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A Critical Review of Studies of the Association between Demands for Hospital Services and Air Pollution

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Studies of the associations between air pollution and hospital admissions and emergency room use are reviewed, including studies of air pollution episodes, time-series analyses, and cross-sectional analyses. These studies encompass a variety of methods of analysis and levels of air quality. Findings from all three types of studies were generally consistent in that almost all of the studies reviewed found statistically significant associations between hospital use and air pollution; this unanimity may have resulted in part from publication bias. These associations were characterized by elasticities of the order of 0.20; i.e., a 100% change in air pollution was associated with a change in hospital use of about 20%, for specific diagnoses. Respiratory diagnoses were emphasized by most studies; cardiac diagnoses were included in five of them. The air pollutants most often associated with changes in hospital use were particulate matter, sulfur oxides, and oxidants. Apart from the major air pollution episodes, there was no obvious link between air pollution level and the significance or magnitudes of the associations. Long-term indicators of hospitalization appeared to also be influenced by medical care supply factors, including the numbers of beds and physicians per capita. These nonpathological causal factors could also have influenced the findings of the time-series studies by introducing extraneous factors in the patterns of admissions. Although consistent associations have been shown between hospital use and air pollution, further research is required to distinguish among potentially responsible pollutants and to deduce specific dose–response relationships of general utility.

Introduction

Much of the extant review literature on the health effects of air pollution is organized by pollutant rather than by type of health response or end point, in part because of the structure of the Clean Air Act. The EPA criteria documents are a case in point (*1*), as well as most toxicological studies, which consider only a single pollutant species or a few combinations, usually at elevated concentrations. In contrast, epidemiological studies are designed to evaluate the responses of populations to the pollutant exposures encountered in the course of their normal daily activities. On a daily basis, many pollutants vary in concert, which can make it difficult for an epidemiological study to separate their effects. Reviewing the epidemiological literature by type of health effect allows a more direct comparison of study methodologies and of the relative effects of different pollutants. A retrospective analysis of this type may be particularly appropriate at this time of heightened awareness of urban photochemical smog problems and of attempting to assess benefits stemming from the recent revisions of the Clean Air Act.

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Increased rates of hospitalization is one of the adverse effects of air pollution. This response was most obvious during the notorious air pollution episodes of many years ago, during which increased rates of mortality were also recorded. Time-series analysis techniques similar to those used for mortality have been used in several studies to try to deduce quantitative morbidity relationships, for example, for rates of hospital admission and emergency room visits. A less common study design has attempted to relate long-term measures of hospital use (admission or discharge rate per capita or length of stay) and air quality on a spatial or cross-sectional basis. This review is intended to place these various studies into a common interpretive framework to examine the degree of consistency and to determine whether an overall pattern of pollutant-specific association is evident.

Respiratory health in the United States can be measured by several different statistical measures, none of which is likely to represent the true "underlying morbidity" of the population. Annual mortality due to respiratory conditions totals about 0.7/1000 population (without age adjustment); annual hospital admissions with respiratory diagnoses, about 13/1000; annual chronic respiratory conditions (bronchitis, emphysema, asthma) total about 70/1000 population (of which about 95% have one or more

physician visit per year); annual acute respiratory conditions occur at the rate of about 1100/1000 population. As an example, Ayres (*2*) reported a winter weekly respiratory case load of 5–8/1000 population for his general practice in Britain, which might equal an annual rate of about 200/1000 when the normal seasonal variation is taken into account. A further example of the range in morbidity statistics may be seen from the data of Richards et al. (*3*) for childhood asthma in Los Angeles; about 14% of cases presenting to the emergency room were admitted to the hospital. The range in these various measures of health response is thus over three orders of magnitude; hospital admissions are in the lower end of this range.

Because mortality variations have been studied extensively in relation to air pollution, it may be convenient to compare these studies with those for hospitalization rates. However, it is important to understand that these two types of observational studies involve different segments of the population. For all causes and ages nationwide, only about 2.5% of hospital episodes end in death in the hospital (*4*). In addition, rates of admission to the hospital can be affected by the availability of beds, on both long- and short-term bases; mortality rates are not affected by such constraints.

Bennett (*5*) presented a brief, mostly qualitative, review of hospital usage studies published through 1979 and illustrated what he considered a number of instances of "misuse" of data on health service utilization as a proxy for the underlying morbidity of the population. He questioned the use of moving averages to eliminate weekly cycles, the assumptions of unchanging relationships over space or time, the effects of individual perceptions as to the seriousness of a symptom, institutional constraints on admissions, adequacy of data reporting, and other extraneous factors that could affect hospital use. However, he did not seem to realize that most of these factors are likely to obscure the nature of any real relationships between the timing of hospital use and air pollution, rather than to create "false positives" as he implied.

This review is intended to be as comprehensive as possible and includes additional studies not considered by Bennett (*5*), including the "gray" literature and more recent publications, and presents a more quantitative approach to the review process. General methodological issues are considered first, followed by reviews of the literature in three groups: episode studies, time-series analyses, and cross-sectional analyses. Some of the more interesting data sets have been reanalyzed, and the findings are summarized in the contexts of overall hospital use statistics and of previous studies of mortality and air pollution. The studies are reviewed by type and by general geographic location, in chronological order.

Study Methodologies

Studies of rates of hospitalization in relation to air pollution attempt to infer dose–response relationships on the basis of concordant temporal or spatial patterns. With severe air pollution episodes, which occur quite rarely, the responses may be obvious in relation to "normal" patterns of hospital use, but when longer time periods are considered, a number of methodological issues may arise. Some of these issues relate to the "ecological" nature of such observational studies, i.e., the attempt to infer effects on individuals on the basis of observations of the behavior of groups. This problem has been recognized in conjunction with "small-area variation" studies of geographic gradients in hospitalization rates (*6,7*), but not specifically in conjunction with time-series studies. For air pollution health studies, the ecological assumption is that persons seeking health services have experienced the same air pollution exposure as the general population at large and that this exposure can be represented by the air quality data available from fixed monitoring sites.

Other statistical problems arising with time-series studies include lag effects, serial correlation, confounding by exogenous long-term trends, and collinearity among independent variables.

Validity of the Dependent Variable Measures

Among the various types of air pollution health effects that have been studied, there are certain advantages to using hospitalization statistics. A visit to a hospital is a voluntary response by the affected individual, based on perceived needs and often after the advice of a physician. Studies of mortality, on the other hand, deal with an inevitable end point and are thus concerned with determining the degree of "prematurity" in addition to cause-and-effect relationships. In addition, because for a given population, hospital admissions are more than an order of magnitude more numerous that deaths, use of this end point facilitates the study of more specific diagnoses.

Most of the studies reviewed in this paper used one of two dependent variables. Some studies dealt with emergency room visits, for which the action taken can be assumed to have been determined solely by the affected individual. Hospital admissions, on the other hand, require the patient to be examined by a physician, which could remove an element of subjectivity from the data (*8*). Admissions are less frequent than emergency room visits by a factor of 2–5; in 1981, the average number of yearly visits to a hospital emergency room or outpatient department for all diagnoses varied from 0.5 to 0.7 per person, depending on age; hospital admissions varied from 0.07 to 0.37 per person. On average, emergency room visits may represent less severe incidents than admissions and thus could conceivably be more sensitive to the effects of air pollution.

Most of the studies examined short-term variation in hospital admissions using time-series methods. However, any significant short-term excess admissions should also be reflected in the long-term statistics (either admissions or discharges) and possibly as differences in lengths of hospital stays. Cross-sectional methods are used to examine differences in long-term averages and must account for a host of possible confounding factors, such as those influencing the supply and delivery of medical care. It also follows that if decisions to hospitalize are influenced by factors other than the patient's immediate needs, short-

term cause-and-effect relationships could be obscured as well.

Reliability of Air-Pollution Exposure Estimates

None of the studies in the literature used personal air pollution monitors or activity patterns to derive detailed estimates of personal air pollution exposure. It was necessary to assume that the time-series of community air pollution monitor readings was an adequate proxy for total integrated exposure [with the possible exception of the Portland, OR, study (*9*)]. This constitutes the "ecological" nature of this group of studies.

Two types of exposure errors are possible: confounding, in which an unmeasured agent is highly correlated with a measured pollutant, and random errors, due to measured indoor pollutants or to randomly located unmeasured outdoor pollutants. To deal with confounding by collinear variables, it is useful to compare similar types of studies in different geographical settings where the associations among collinear variables are likely to differ, which is one of the objectives of this review. Random errors in independent variables, on the other hand, will usually bias any derived correlations or regression coefficients downward. Thus, one could expect that the dose–response relationships derived by studies using imprecise pollution measures will be underestimates of the true effects, *ceteris paribus*.

Use of Control Diagnoses

Controls are intended to test for "false positives," i.e., statistically derived associations between health measures and air pollution that are physiologically implausible. In studies of air pollution episodes, the population serves as its own control in that it is expected that its health status will return to normal values after the episode has abated. For time-series studies, those diagnoses that are unlikely to respond to air pollution (or those populations that are known to be unexposed to the pollutants in question) should be considered as candidates for controls.

Confounding Variables

All time-series studies of air pollution effects must take into account the natural temporal patterns in air quality, which can confound statistical analyses if the response variables have similar patterns that could conceivably be due to other factors. These include both long- and short-term patterns. On a long-term basis, seasonal trends include higher ozone levels in summer and higher levels of pollutants associated with space heating in winter. Such seasonal cycles may be confounded with seasonal weather cycles, which can also affect health responses. Respiratory illness shows a seasonal pattern; it is higher in winter, in part because of periodic outbreaks of viral infections (*10*). There may also be longer-term air quality trends associated with community growth or with air pollution abatement efforts. Weekly cycles may be expected in traffic-related air pollutants or in those pollutants related to local industrial sources that operate with reduced emissions on weekends. Hospital usage also tends to exhibit weekly patterns, often because of the reduced availability of physicians on weekends. Emergency room usage is frequently higher on weekends, whereas admissions are usually reduced.

One of the traditional methods of avoiding such temporal confounding is the use of deviation variables, i.e., the difference between the observed value and the value expected for that day of week, season, year, etc. This practice is essential for the dependent variables; its use for the air pollution variables is tantamount to assuming linear responses, which are often assumed by the use of linear regression models in any event. A metric in less common use for studying specific diagnoses, such as respiratory disease, is the percentage of all diagnoses represented by the selected category. This implicitly assumes that the confounding variables such as day-of-week are randomly distributed among all diagnoses, which may not always be a valid assumption.

Autocorrelation

Tests of significance of regression coefficients require that the residuals be uncorrelated. This condition is frequently violated in both time-series (presumably because of meteorological persistence) and spatial analyses (because of regional similarities of neighboring cities), with the result that significance levels can be overstated. In time-series analysis, the phenomenon is called serial correlation, and formal methods have been developed to deal with it. Hammerstrom et al. (*11*) showed that confidence limits on bivariate correlation coefficients averaged about 7% wider when based on bootstrapping, as opposed to the classical method based on the z-transformation. Because autocorrelation effects could be larger than Hammerstrom et al. found, if serial correlation has not been accounted for, the alpha level for hypothesis testing should be decreased, say from $p < 0.05$ to $p > 0.01$, to be conservative (*8*).

Selection of Lag Periods and Averaging Times

Most time-series studies use daily data, which is the shortest time period for which hospitalization data are usually recorded. Aggregating to longer periods is one way of reducing the effects of Poissonian variability in the dependent variable, at the risk of losing the details of the time–response patterns. Some studies have used weekly or monthly data, for example. When daily data are used, it is important to account for lags between stimulus and response. It may be unreasonable to expect an affected person to be hospitalized on the day of exposure except in the most severe cases; a lag may result from either the unavailability of a hospital bed or of the appropriate physician. Moreover, it is likely that there will be a range of such lags in a heterogeneous population. One way of capturing the total response to an air pollution event is to

add the admissions for some number (n) of succeeding days. For a stationary time series, this is equivalent to adding or averaging the pollution over n days before admission. Such a summation accounts for the "harvesting" effect that is sometimes indicated when the longer lags tend to be negative, as well as the tendency for the total response to be split over the various lag periods (which reduces the significance of any individual lag variable). An approximate estimate of the significance (t value) of the sum over lags may be obtained from a multiple regression by adding the coefficients and dividing by the average standard error.

Because air quality data for many species are often available on an hourly basis, the analyst must decide whether to use daily peaks or daily averages as the measure of the effective dose. If a nonlinear or threshold type response is expected, daily peak values would be appropriate for a physiological model. This would also be the case if the peaks occur during a time of day when outdoor exposure is more likely. However, there are other factors to consider in making this choice to distinguish between statistically effective and physiologically appropriate doses. First, the peak value may only apply to a localized area around the monitoring station and thus may not be representative of the entire community. Daily averages tend to be smoother spatially and thus more representative of average community levels. Second, if it is desired to compare regression or correlation results among various pollutants, it is essential that data for all pollutant species be based on the same averaging time in order to compare on the basis of equivalent random noise levels and spatial representativeness. Differences in the "noise" in the independent variables can bias the comparison of regression statistics. Because most particulate mass data are only available for 24-hr samples, daily averages may be the least common denominator for the purpose of comparing models using alternative pollutants.

Measures of Association

The correlation coefficient is perhaps the most commonly used measure of association between two variables, but its magnitude is sensitive to the number of observations in the data set. In addition, bivariate relationships are often confounded by intervening variables such as season or weather (for temporal analyses). Some authors have used contingency tables and the chi-square test to establish significant differences. Where possible, multiple regression analysis has been used in this review to try to separate the effects of air pollution from potential confounders. Regression coefficients may be presented in terms of physical (scaled) units such as cases per microgram per cubic meter, but nondimensional units facilitate comparison among pollutants and situations. The elasticity is a nondimensional form of regression coefficient that can be calculated (at the mean) for a linear model as

$$e_i = b_i(\bar{x}_i/\bar{y}) \qquad (1)$$

This equation represents the change in the dependent variable for a specified change in an independent variable and is usually stated in percentage terms in this review. Because the correlation and regression coefficient are related by $b = R\,(s_y/s_x)$ (for a bivariate relationship) and the coefficient of variation (CV) is $s/\bar{x}$, then $e = R\,(\mathrm{CV}_y/\mathrm{CV}_x)$. Data from some of the other studies reviewed below suggest that CV is about 0.3 for admissions and about 1 for short-term air pollution data.

Reviews of Published Studies

Studies of Air Pollution Disasters

Air pollution disasters or "episodes" lasting only a few days allow more detailed examinations of the time course of events than any other type of study. However, the rarity of these events and the accompanying high concentrations of pollutants may make extension to the more general case somewhat problematic.

Donora, Pennsylvania. The Donora disaster in October 1948 affected a high percentage of residents and was studied extensively, albeit retrospectively (*12*). No concurrent air monitoring was performed. Of the 50 persons hospitalized (compared to 20 deaths), records were available for 34, and two of these were workers on riverboats that were passing by Donora. This suggests that prior chronic exposure, which might be assumed for residents, was not a prerequisite for susceptibility to this incident. Based on the available hospital records, Shrenk et al. (*12*) found no diagnostic information that related directly to air pollution; all of the findings were attributed to other disease conditions present. For example, "... all patients appeared to have in their clinical histories a component of cardiorespiratory disease" (*12*).

London. London was well known for its polluted fogs from at least the 19th century, if not earlier. The data collected in December 1952 and December 1957 lend themselves to detailed analysis of mortality and hospitalization. The most useful measure of hospitalization rate is "requests for emergency bed service" for Greater London (*13,14*) because this measure accounts for possible supply constraints due to unavailability of beds. These figures account for about 25% of daily admissions under normal conditions.

The episode of December 1952 in London appears to be the first for which both air quality and health response data were collected. Fog persisted for 5 days and smoke and SO_2 levels exceeded 4000 $\mu g/m^3$ locally in central London; Meetham (*15*) estimated that sulfuric acid and CO levels would also have been elevated, although no measurements were made of these species. The winter average of emergency bed requests for acute (noninfectious) cases was about 150–180 per day (*16*). When the episode began on December 5, weekly admissions were already elevated above normal levels (>200 per day) for reasons that may relate either to weather or to an excess in the numbers of pneumonia cases (*14*). The peak daily emergency bed request was reported to be 492 on December 9 (an excess of about 150%) on the day after the peak pollution was recorded. These figures compare to a daily average of 750

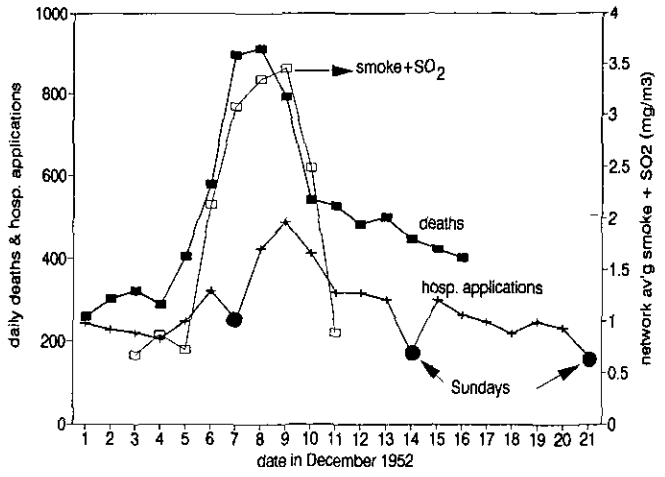


FIGURE 1. Time line for the 1952 air pollution episode in London, showing deaths, emergency applications for hospital beds, and air pollution based on network averages. Data from British Ministry of Health (*14*).

acute respiratory hospital admissions for the week preceding the fog and an increase to 1110 on December 9, of which 460 were for respiratory disease. Weekly admissions did not return to the pre-episode level until December 25. Most of the excess applications were for respiratory diagnoses, which increased by a factor of 4. Cardiac disorders tripled, but from a much lower base level. By age, most of the increase was reported for the less-than-5 and over-45 year age groups.

The time histories of mortality, emergency hospital bed applications, and the sum British smoke and SO_2 are plotted in Figure 1. Air quality data are based on the 24 hr ending at noon on the day in question. Because they tend to be highly correlated during London winters, values of smoke and SO_2 have been added to provide a crude index of the combined pollution effect during the episode, for the purpose of illustration. The increases in smoke and SO_2 were reasonably coincident; the period of heavy fog lagged air pollution by about 2 days (perhaps because the polluted air contributed to fog formation). Mortality lagged air pollution by about 1 day (actually by 1.5 days). Hospital applications increased more slowly and stayed elevated after the fog (note the periodic dips in hospital applications on Sundays; I used an additive correction of 100 for the Sunday values for the purpose of estimated dose–response curves). These pollution data are based on the average of 11 stations for smoke and 10 for SO_2; the average values are considerably lower than the figures that are usually used to characterize this episode (4000+ $\mu g/m^3$).

Cross-plots of these data are given in Figure 2*ab* for various assumed lags between pollution and response; the arrows indicate the direction of increasing time. This model assumes an average response over a period of k days after the pollution measurement. Note that the peak pollution levels occurred on the weekend during this episode, during which only 48-hr samples were taken at most of the air monitoring stations. Thus, the dose–response curves should actually pass through the average response (indicated on the graphs) for the 2 peak pollution days. Figure 2*a* plots mortality and morbidity responses for assumed lags of 2 days. The mortality responses form a reasonable dose–response curve except for the last day, which shows that excess mortality persisted beyond the assumed 2-day lag. Hospital applications did not form a linear dose–response relationship for this lag. Figure 2*b* presents these same data for a lag of 3 days for mortality and 5 days for morbidity, which results in more conventional-looking dose–response curves. The non-dimensional slopes or elasticities of these dose–response relationships that are about 70% for mortality and 50% for

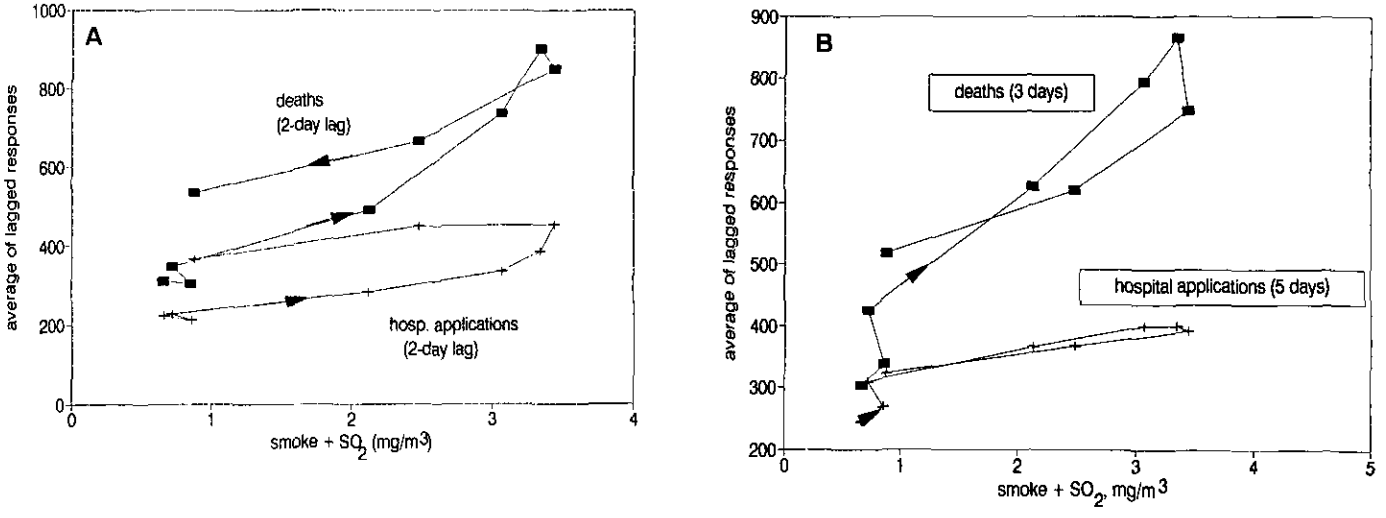


FIGURE 2. Dose–response functions for the 1952 London episode, for mortality and hospital applications, based on the sum of smoke and SO_2. (*A*) Lagged 2 days, (*B*) with a 3-day lag for mortality and a 5-day lag for hospital applications. Data from British Ministry of Health (*14*). Arrows indicate the direction of increasing time.

morbidity. It is noteworthy that, in spite of the severity of this episode, "excess" deaths exceeded "excess" hospitalizations (as measured by emergency requests), which suggests that the primary mechanism may have been exacerbation of existing disease.

These dose–response relationships are seen to resemble either of two types of patterns, depicted schematically in Figure 3. When the assumed lag period is too short, the response persists after the pollution has abated. When it is too long, there is an induction period at low pollution levels during which the response seems to increase precipitously with only minimal changes in pollution. The patterns of Figure 2 thus seem to indicate that during a severe episode, the lag increases during the course of the episode, probably because the most susceptible individuals respond first. If an attempt is made to define such an episode by means of a linear slope, it appears that use of insufficient lag will underestimate the slope (with a reduced correlation coefficient), and excessive lag may either overestimate the slope or indicate a quadratic relationship with leveling off at higher pollution levels.

Fry (*17*) reported the impact of the 1952 fog on his general medical practice (4500 patients) in the southeastern outskirts of London for the week of the episode; upper respiratory tract complaints increased by about 150%, while "respiratory disorders" (all conditions with symptoms referable to the lungs and where abnormal signs were detected) increased by about 400%. The increased patient load continued for at least another week, having begun on the third or fourth day of the fog (corresponding to maximum pollutant concentrations). Fry identified 43 patients with lower respiratory tract involvement, 37 of whom had a history of previous chest trouble. These were concentrated in the age group 60–80 and consisted of 29 men and 14 women. He considered 16 of these to be severely ill; of the remainder, "quite a number . . . were able to remain up and about in their homes and some even went out to work" (*17*). Two of the group died within 8 days and one was admitted to the hospital. Fry reports that none of his pediatric asthmatic patients was affected by the fog episode.

The Ministry of Health report (*14*) shows an increase in upper respiratory disorders of about 100% lasting at least 2 weeks after the incident. Fry also reported that six patients were seen with sudden attacks of vomiting at the peak of the fog, not accompanied by other gastric symptoms. He concluded that the cause was related to "swallowing fog." This was also the case at Donora, where some instances of gastric distress were reported (*18*). If Fry's somewhat anecdotal report could be taken as representative, one would conclude that many more people suffered symptoms from the episode than either died or were admitted to hospital (but nevertheless, only a small fraction of the total population was seriously affected).

The January 1956 fog in London (and elsewhere in England) was somewhat less severe because only one 6-hr period of visibility less than 100 m was recorded (*19*), and there were far fewer casualties (*20*). The reported morbidity data (*20*) included the increase in claims for incapacity benefits" for 2-week periods, which was about 70% for Greater London and the southeastern region and 41% for the remainder of England and Wales. The difference between these two figures may represent the local morbidity effect of the fog.

In December 1957, London was again struck by a 4-day polluted fog episode (*19*). Average pollution levels were about 25–30% lower than 1952 when based on a common set of measuring stations, but the fog was not as thick, and visibility was severely restricted for a smaller fraction of time. Also, calm winds were reported much less frequently in 1957. Excess mortality was only about 20% of that experienced in 1952. Figure 4 presents the time histories of the various parameters; these trends are qualitatively similar to those from 1952 (Fig. 1) in that both deaths and hospital applications lag pollution by days, and hospital admissions are low on Sundays. I attempted to compensate for this by adding 50 applications to each Sunday's total for the purpose of plotting dose–response curves (Fig. 5). The

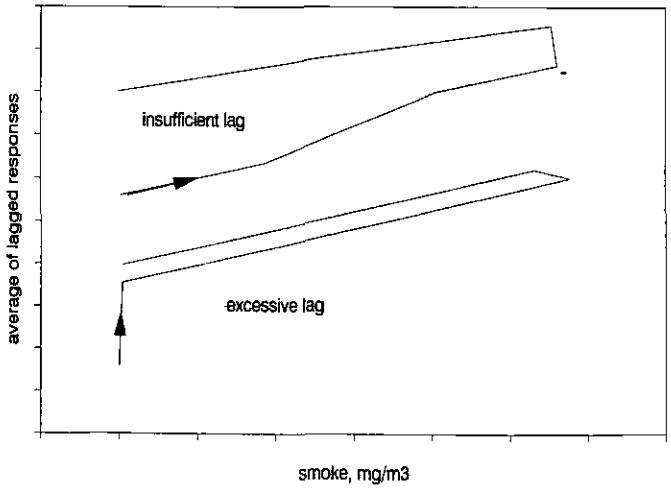


FIGURE 3. Examples of typical dose–response functions for various lags.

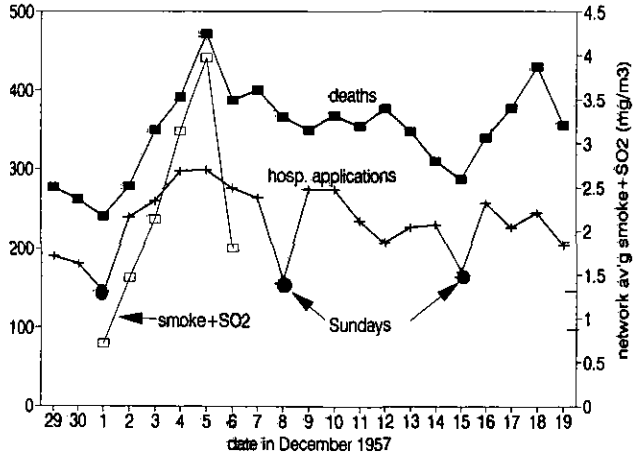


FIGURE 4. Time line for the 1957 air pollution episode in London, showing deaths, emergency applications for hospital beds, and air pollution (network average). Data from Bradley et al. (*19*).

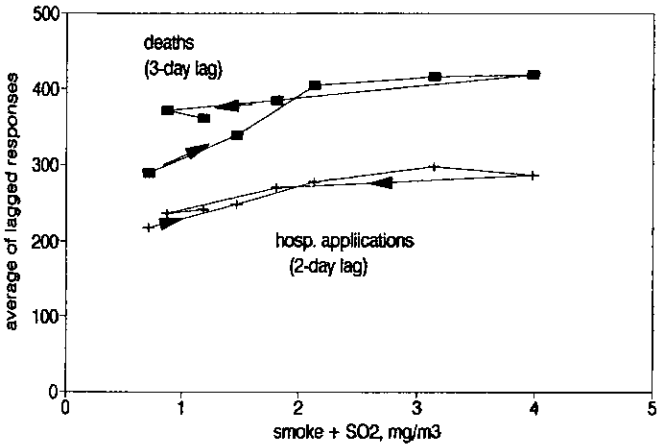


FIGURE 5. Dose–response functions based on the sum of smoke and SO_2 for mortality and hospital applications, with a 3-day lag for mortality and a 2-day lag for hospital applications, during the 1957 London episode. Data from Bradley et al. (*19*).

most consistent dose–response curve for hospital applications was based on the sum of smoke and SO_2 with a 2-day lag; the elasticities for both deaths and hospital applications were about 20%.

It is difficult to answer the question of why the 1952 fog was so much more lethal than the 1957 fog. They both lasted several days and had peak smoke levels over 4 mg/m^3, at least in local areas. Temperatures were similar but slightly colder than in 1952. The available air quality data show that the high smoke concentrations in 1957 occurred in outlying areas, apparently because of light, persistent winds; perhaps fewer people were affected there. The levels of fog and of ventilation would appear to be additional important factors. For example, the extremely low level of visibility during the 1952 fog was reported to have drastically slowed transportation, which could have hampered attempts to seek medical assistance and could have had an effect on the survival of some of those affected. There were 4 consecutive days of calm winds in 1952, during which levels of all pollutants (including carbon monoxide, for example) would have continued to build up. H_2SO_4 was probably formed in the 1952 fog, but the lack of a noticeable decrease in SO_2 gas concentration (due to absorption by the fog) compared to smoke as the fog intensified appears to rule out a substantial amount of SO_2 oxidation. In addition, mortality in 1952 had already started to increase before the fog became intense. The most likely answer to this question is therefore inadequate characterization of the actual population exposures to air pollution, although it is also possible that the publicity given the 1952 incident caused the public to take aversive action during the 1957 episode (as they were reported to have done in 1962).

Few morbidity data were reported from the 1962 episode in London, during which SO_2 levels exceeded those reported in 1952, but smoke levels were considerably lower. Marsh (*22*) reported a 50% increase in new sickness benefit claims. Waller et al. (*23*) showed a sharp (1-day) peak of about 100% in emergency bed applications coincident with the day of maximum air pollution; the mortality peak was only about 40%, but lasted for 3 days. This report (*23*) also shows a less severe event in January 1963; the emergency bed application response to both of these peaks was about 3% per 100 μg/m^3 smoke. When referred to SO_2, the responses were about 2.6% and 1% per 100 μg/m^3, respectively. These figures are comparable to the slopes of Figure 2.

Effects of the 1962 fog on the workload of general medical practitioners were reported by Carne (*24*) as part of an analysis of pollution and weather effects for the winter seasons of 1962–1964. Corresponding air quality data for episodic events were reported by Waller and Commins (*21*). These two data sets have been combined in Figure 6, which plots weekly timelines for new cases of respiratory diseases ("onsets"), and physicians' consultations for either respiratory disease or other causes. The pollution data are the maximum daily values for the event; the "H+" data represent the total acidity of the aerosol reported in equivalent units of H_2SO_4 in micrograms per cubic meter. The December 1962 fog is seen clearly in terms of a sharp peak in onsets and a broader peak for respiratory consultations (Figure 6*a*). There is a sharp coincident drop in nonrespiratory consultations; this could be interpreted as a supply constraint or perhaps that people did not wish to venture out during these adverse atmospheric conditions. Such aversive behavior was mentioned by Marsh (*22*) and by Scott (*25*). The sharp drop in consultations at Christmas is notable as is the broad increase at the beginning of February. No peaks are seen corresponding to the other two air pollution "episodes" of this season (although the first one could have been obscured by the general rise in respiratory effects at that time); their pollution levels were considerably lower. Corresponding data for the winter of 1963–1964 are plotted in Figure 6*b*. The effects of the one episode indicated by Waller and Commins (*21*) can barely be discerned, but the pollution levels were modest (in terms of normal London levels).

New York City. The first reported air pollution episode in New York occurred in November 1953; the lack of atmospheric ventilation caused smoke levels to reach a COH value greater than 8.0, and SO_2 reached 0.85 ppm; fog was reported sporadically (*26*). The total suspended particulate (TSP) sampler routinely operated by the National Air Sampling Network (NASN) recorded in a 24-hr average of 642 μg/m^3 during this event. Widespread complaints of eye irritation were reported, and data on visits to emergency room clinics at four of the city's hospitals were analyzed (*27*). The numbers of emergency clinic visits for each of four hospitals before, during, and after the episode were calculated, and it was concluded that statistically significant increases were seen for upper respiratory infections at three of the four hospitals and for cardiac diagnoses at two hospitals. The New York stagnation episodes were generally characterized by increased temperatures, in contrast to London where episodes were usually accompanied by colder weather.

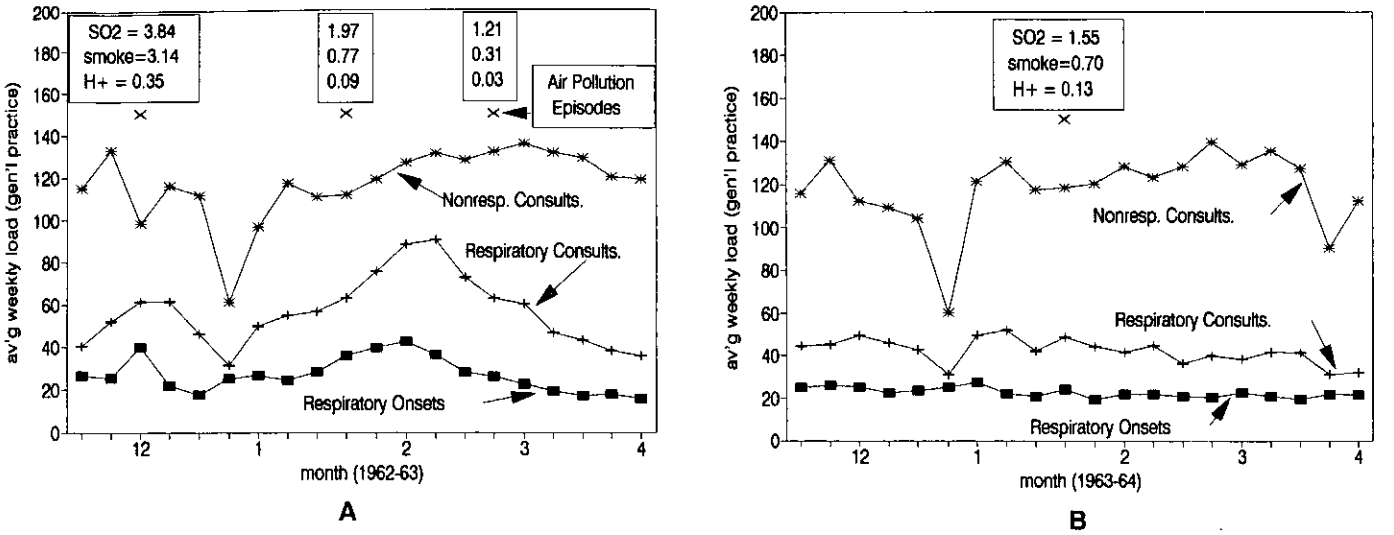


FIGURE 6. Time lines of morbidity indexes during the 1962 and 1963 London episodes (indicated by the air pollution levels at the top of each plot). (*A*) winter of 1962–1963, (*B*) winter of 1963–1964. Data from Carne (*24*).

I reanalyzed this event by pooling the visits to all four hospitals and analyzing them as a single daily time series with varying lags. Day of week was accounted for but temperature was not; the short time span of the analysis (29 days) makes it unlikely that seasonal trends could have interfered. Because day-of-week effects were marginal, the analyses were performed as bivariate regressions, using either smoke or SO_2 as the dependent variable. The SO_2 monitoring record was fragmentary (data available about 2 hr per day, morning and afternoon, for 10 days), which made it impossible to discriminate between the two pollutants on the basis of these data alone. The results are presented in Figure 7. Respiratory clinic visits appeared to be associated with either SO_2 or smokeshade,* with no lag (Fig. 7*a,b*). Cardiac visits fit better with a 3-day lag (Fig. 7*c,d*). The largest percentage response is seen for cardiac causes, although the absolute numbers are small (13 visits per day for the four clinics). The three smoke-shade relationships are statistically significant ($p < 0.01$). Regressions using the data grouped for three periods in November 1953 and the averages of the Novembers of 1950–1952 and 1954–1956 gave similar results. Assuming that the many other hospitals in New York had similar responses, the morbidity effect would appear to have been larger than the mortality effect during this episode (about 200 excess deaths or about 9%) (*27*).

In December 1962, similar air pollution levels were recorded in New York, but for intermittent periods over 8 days (*28*). Sulfur dioxide reached 1.4 ppm for several hours but dropped to normal levels each day; smoke shade was elevated on a more persistent basis, reaching about 8 COHs. Mortality counts and visits to six clinics were analyzed, plus data from Blue Shield (insurance claims) and four old-age homes. Again, the statistical technique was to compare grouped time periods; the authors report significant increases during the episode only for the old-age homes (it was not clear how the tests of significance were performed). Because the authors did not report daily morbidity data, it was not possible to perform a reanalysis. It appeared that the sum of morbidity responses across all institutions was elevated during the episode period. A reanalysis of the mortality data showed a nearly significant association with smoke shade with about the same slope as in the 1953 episode.

Data from the 3-day Thanksgiving 1966 episode in New York (*29*), during which smoke reached about 600 $\mu g/m^3$ and SO_2 reached 1300 $\mu g/m^3$, were confounded by the closing of the outpatient clinics on the holiday (Thursday). This may have created an increased patient load on the emergency rooms, which showed excess use only on Friday, at the end of the episode. Thus, the excess could have resulted from the perturbation caused by the holiday. The numbers of emergency room visits were small, however; the excess respiratory visits totaled about 40%, based on an average of the holiday and the day after.

Los Angeles, 1954. Periods of high air pollution were experienced in the Los Angeles basin in the fall of 1954 (*30*). The initial report focused on the period October 15–20, during which oxidants increased about 15% over the control period; no consistent relationships with mortality or morbidity could be found. However, examination of the published raw data shows two spikes in particulates on October 8–10 and on November 4 (from normal levels of about 200 $\mu g/m^3$ to 500–650 $\mu g/m^3$ at Pasadena). The periods of highest hospital admissions for all diagnoses and for asthma were October 16 and November 6 (asthma admissions were approximately doubled). In general, there were no anomalous temperatures during this period, except for an increase of about 10–15°F on November 5, to

*"Smokeshade" is the term used in the United States for certain measures of particulate matter based on staining of filter paper and is similar to "British smoke."

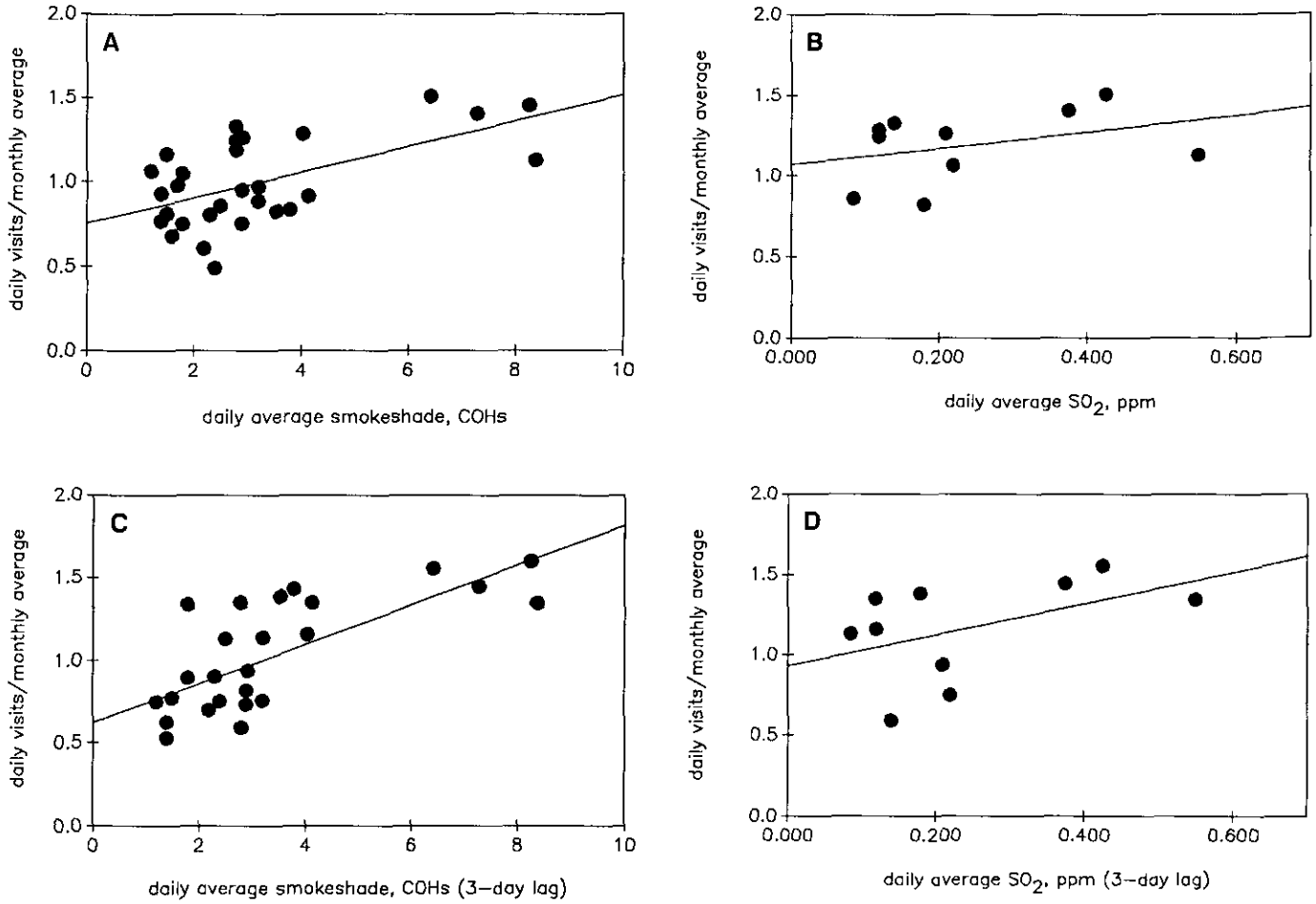


FIGURE 7. Dose–response functions for emergency clinic visits during the 1953 air pollution episode in New York City. (*A*) respiratory visits, based on smoke shade, (*B*) respiratory visits, based on SO_2, (*C*) cardiac visits, based on smoke shade, (*D*) cardiac visits, based on SO_2. Data from Greenburg et al. (*27*).

85°F. Other morbidity measures also peaked during these 2 weeks. This response is consistent with a lag of a few days, which had apparently not been considered by the original authors.

Pittsburgh, 1973. An air stagnation event occurred near Pittsburgh in August 1973, with 24-hr TSP levels around 400 $\mu g/m^3$ (*31*). Sulfur dioxide reached about 340 $\mu g/m^3$ (R. Savukas, Allegheny County Bureau of Air Pollution Control, personal communication, May 1989). Using Medicare records, Shiffer and Parsons (*32*) deduced an increase in respiratory hospitalizations during this 13-day period compared to the 2 previous years (35 admissions versus 13 and 21, respectively). They also noted four deaths following hospital admission with a respiratory diagnosis, which was more than the previous years, but too few for reliable statistics.

Mount St. Helens Volcanic Eruption, 1980. In May and June 1980, volcanic eruptions blew ash into the stratosphere and increased atmospheric suspended particulate levels over a wide area, with ash deposition levels of up to two inches in Spokane County, Washington, and elsewhere in the region. Most of the ash was of respirable size, although the fine particle fraction mass was only around 100 $\mu g/m^3$ (*33*). Total suspended particulate levels were much higher, up to 30,000 $\mu g/m^3$ in the plume (*34*). There was little sulfur or chlorine in the ash, and the pH after solution was essentially neutral (*33*).

At least 18 people died in the impact zone due to asphyxia from ash inhalation (*34*); the population at risk was not reported, but the 150-square-mile was described as "largely uninhabited." Kraemer and McCarthy (*35*) reported that Spokane residents complained of eye and throat irritation and that local hospitals experienced increased pediatric asthma admissions. Comparing 1980 with 1981 hospital admissions showed an excess of 34% for the year, but not all of this excess was associated with the eruption. The 1980 admissions rate for May was double that of 1981, but this was also the case for the month of April (before the eruption). A regression of monthly percent excess asthma admissions against the monthly average difference in TSP was not statistically significant, although the regression coefficient was similar in magni-

tude to that estimated from other episodes and studies. As a time-series analysis without reference to a normal year for standardization, TSP would undoubtedly be a significant predictor. Biweekly pediatric asthma admissions responded to TSP spikes of about 1,000 and 10,000 $\mu g/m^3$ with approximate doubling in admission rates (in both cases).

Following the first eruption, Baxter et al. (*34*) reported increased emergency room visits and admissions in eastern Washington by about a factor of 3 for respiratory diseases in the first week and persisting for 4 weeks. After the May 25 eruption, the local increase was about 100%. They also reported that some patients who initially had breathing difficulties were later diagnosed with cardiac problems. The largest category of respiratory emergency room visits was for asthma/wheezing.

Tests of children's lung function found essentially no effects due to deposited ash (*36*); this evaluation was based on tests conducted at a summer camp after the eruption at which average respirable dust levels were around 170 $\mu g/m^3$. This may indicate that only certain susceptible individuals were affected by the ash.

Baxter et al. (*37*) studied emergency room utilization over a 4-week period associated with this episode in Yakima, Washington, and noted a doubling for asthma and bronchitis visits. The rate tripled for the first week of the episode. A case–control study of these patients showed them to be characterized by a previous history of asthma or bronchitis, rather than by additional exposure to particulates. Buist et al. (*38*) studied a group of occupationally exposed loggers for 4 years and found no lasting changes in lung function as a result of their exposures. They had shown a significant, exposure-related decline in lung function during the first year after the eruption.

Note that because the Mount St. Helens incident did not involve excess SO_2, these data imply that SO_2 is not an essential ingredient of the community air pollution mix with respect to excess respiratory hospitalizations.

West Germany, 1985. Wichmann et al. (*39*) reported that about 19% excess hospital admissions were recorded during a 5-day episode in central Europe in January 1985. Peak smoke levels reached 850 $\mu g/m^3$ (3-hr average) and SO_2 reached 2170 $\mu g/m^3$ (30-min average). Maximum 24-hr average values of NO_2 and CO were 230 $\mu g/m^3$ and 7 ppm, respectively. The excess hospital admissions were all due to cardiovascular causes; no significant increase was seen in respiratory admissions. In a multiple regression model for the sum of respiratory and cardiovascular admissions, which included the effects of temperature, results were much more significant when a 2-day lag was used for smoke, SO_2, NO_2, and CO (daily averages).

This data set also allows a comparison of the absolute numbers of deaths, hospital admissions, and consultations in physicians' offices. The numbers of hospital admissions for cardiovascular and respiratory causes were about the same order as the numbers of deaths (more for respiratory; fewer for cardiovascular). The number of physicians' consultations was 100–500 times the number of deaths, but no correlation was found between air pollution and physicians' consultations.

Northern California Forest Fires, 1987. Dry lightning strikes ignited more than 1500 forest fires in Northern California during a 5-day period in August–September 1987 (*40*). Total suspended particulate readings reached more than 4 mg/m^3, and local visibility was reduced by 90% for several days. Data were gathered on emergency room visits in six counties, and the effects of the fire were assessed by comparing the numbers of respiratory visits with the numbers that would normally be expected at that time of the year (ratio of observed to expected; O/E). Significant excesses were shown for asthma (O/E = 1.4), chronic obstructive pulmonary disease (O/E = 1.3), laryngitis (O/E = 1.6), sinusitis (O/E = 1.3), bronchitis (O/E = 1.2), and other upper respiratory infections (O/E = 1.5). The excess emergency room visits for pneumonia, tonsillitis, pharyngitis, mental health problems, and bee sting reactions failed to reach significance. Excess emergency room visits for coronary problems and otitis were nearly significant ($p = 0.1$). Because this is a relatively sparsely populated area with no routine air pollution monitoring, it was not possible to estimate air pollution exposures.

Summary of Episode Morbidity Studies

These air pollution episodes span a range in levels of air quality and in responses. Respiratory diagnoses were the only category of admissions evaluated in all studies. Figure 8 plots these responses against daily maximum smoke concentrations (the Mount St. Helens point is plotted at the log mean of 1000 and 10,000 $\mu g/m^3$; two data points are shown for London, 1957, corresponding to the maximum daily smoke reading, which occurred in the outskirts of the city, and the highest central city reading). The Pittsburgh episode is clearly an outlier on this plot, but since fewer than 20 excess admissions were recorded for this episode, this datum is quite uncertain. Similarly, the New York data point may be an upper limit because the potentially confounding effect of the holiday was not removed. On a logarithmic plot basis, the slope is not significantly different from unity, implying a linear relationship. Plotted in linear coordinates, the slope is about 3–

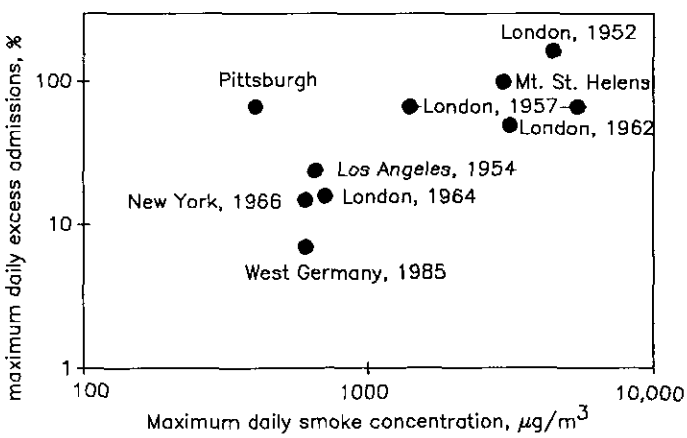


FIGURE 8. Comparison of morbidity responses during various air pollution disasters, based on maximal measures.

4% excess respiratory admissions per 100 $\mu g/m^3$ of smoke. The use of smoke (alone) as a correlating parameter is an arbitrary choice; for example, if SO_2 were added to smoke as in Figure 2, all of the points would shift to the right except the Mount St. Helens datum. We also note that data from the Northern California forest fire disaster are consistent with Figure 8 (30–40% excess visits and particulates probably in excess of several hundred micrograms per cubic meter).

Time-Series Studies

London. In his analysis of winter fogs in London during the late 1950s, Martin (*41,42*) studied deviations from 15-day moving averages of deaths and of emergency requests for hospital admission. He noted that morbidity was less sensitive than mortality, was unable to separate smoke effects from SO_2 effects, and found bivariate correlation coefficients in the range of 0.25–0.34 for respiratory conditions, 0.20–0.28 for cardiovascular conditions, and 0.17–0.32 for all causes. Log transforms were used for the pollution variables in calculating these correlations, but lag periods were not considered (beyond that inherent in the pollution data reporting convention, i.e., 24-hr averages ending at 9 AM on the day of reporting). Day-of-week effects were removed using a statistical adjustment procedure, which resulted in a 35% increase in Sunday admissions requests, for example (*41*).

Martin (*41,42*) tabulated mortality and morbidity (respiratory and cardiac) data for selected high pollution days during the winters of 1958–1959 and 1959–1960. The health response data were on a same-day basis, and days preceded by days of higher pollution were eliminated by Martin to preclude confounding by lag effects. I replotted these data in Figure 9; Figure 9*A* plots data for 26 days in which both smoke and SO_2 were high, using their sum as a correlating parameter as in Figure 2. The mortality and morbidity responses are cross-plotted in Figure 9*B*; after allowing for the fact that the morbidity measure used here (emergency bed applications) accounts for only about 20% of admissions, the figure suggests that for this data set, the "excess" mortality and morbidity responses to air pollution (as measured by hospital admissions), are approximately equivalent. Martin did not consider lag effects, and thus probably underestimated the relationships between episode mortality and morbidity and air pollution. Because no absolute values were given, elasticities cannot be calculated with confidence; if the 1952 winter normal value of 200 per day is used (based on the Emergency Bed Service), the elasticity values for linear dose–response functions would be 5.7, 7, and 6.7% for smoke, SO_2 and their total, respectively. Elasticities for mortality were higher, especially for smoke. Consideration of lag effects would probably have increased these values considerably. Neither Martin's tabulated data nor the scatter plots suggested the presence of pollution thresholds.

Holland et al. (*43*) also studied London hospital admission data for 1958 in relation to smoke concentrations and certain weather variables on a monthly average basis. They found significant effects for smoke with respect to respiratory admissions (but not heart disease), only for ages over 15, together with a significant negative effect for mean daily temperature. The same technique was used for a data set for Royal Air Force personnel in various locations; only the temperature effect was replicated (smoke levels were described as "low," but values were not reported).

Studies in California. Hospital admission patterns in Southern California have been studied since the 1950s, primarily in conjunction with air pollution by oxidants. The first such study (*44*) examined a 4-month period in 1954 and failed to find significant associations between any of several admissions categories and weekly oxidant levels. Brant and Hill (*45*) performed a similar short-term study for the same time period and claimed to have found a significant relationship with oxidant levels lagged by 4

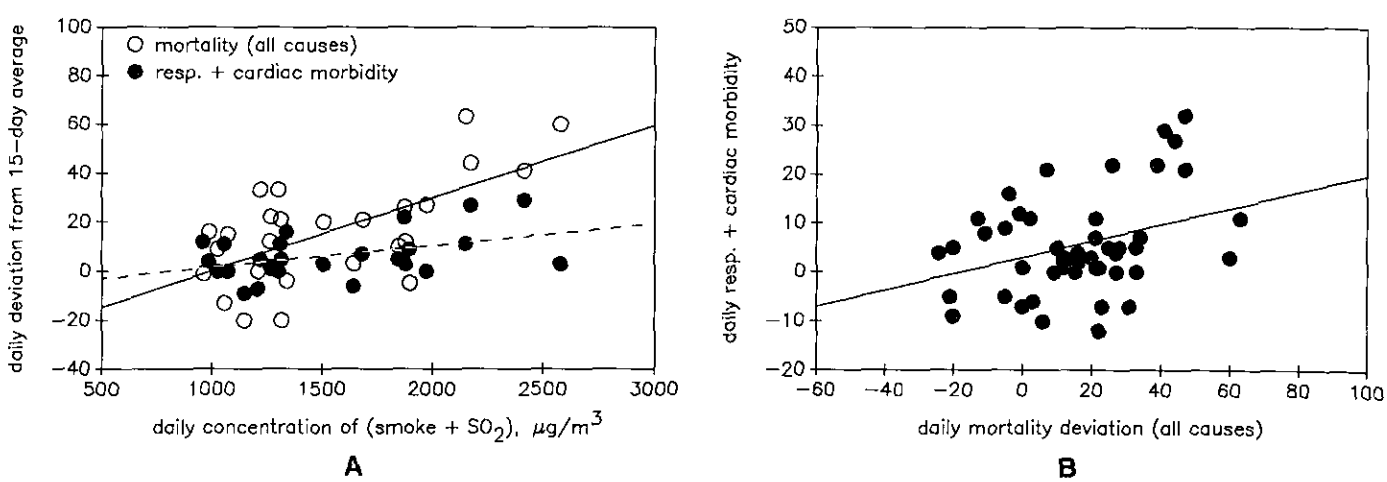


FIGURE 9. Dose–response functions for mortality and emergency bed applications in London, for the winters of 1958–1959 and 1959–1960, based on the data of Martin (*41*). (*A*) Based on the sum of smoke and SO_2, (*B*) cross-plot of morbidity versus mortality responses.

weeks. However, their study used a small number of observations in relation to the number of independent variables and cited 24-hr oxidant levels in the range of 1–2.8 ppm (about an order of magnitude too high). For these reasons, I chose to disregard their findings.

The Los Angeles studies by Sterling and colleagues (*46–48*) appear to be more credible. In their first study (*46*), they examined 223 successive days from March to October 1961 for relationships with day of the week, weather and air pollution: oxidants, ozone, SO_2, NO_2, CO (often labeled as CO_2 in the paper), NO, NO_x, particulate matter (apparently COH), and "oxidant precursor." Pollution data were obtained from eight monitoring stations about 5 miles apart; hospital admissions were used from all hospitals with more than 100 beds located within 5 miles from an air monitoring station. Apparently, all locations were pooled to provide a single time-series data set, resulting in a total of about 30,000 admissions (an average of about 134 per day).

Because admissions and pollution showed noticeable day-of-week patterns, both were adjusted for day-of-week by taking residuals from the overall average for that day. Admissions were grouped by degrees of "relevance" to potential air pollution effects: "highly relevant" diagnoses included allergic disorders, inflammatory diseases of the eye, acute upper respiratory infections, influenza, and bronchitis (about 5/day or 3.7% of the total); "relevant" diagnoses included diseases of the heart, rheumatic fever, and vascular diseases, and other diseases of the respiratory system (about 17 per day); "total relevant" diagnoses were defined as the total of the above; "irrelevant" diagnoses constituted all others.

Correlations were presented for these deviation variables; no seasonal corrections were made. Statistical significance ($p < 0.01$) was shown for all pollutants versus highly relevant diseases (except for SO_2, for which $p < 0.05$). For the relevant diseases, CO, NO_2, NO_x, oxidant precursors, and particulates were not significant, whereas SO_2 and ozone remained significant. Neither temperature nor humidity was significant. Irrelevant causes showed negative relationships. For the total relevant grouping, ozone, SO_2, and total oxidants had the highest correlations (0.25–0.27). Correlations for total admissions (all causes) were mixed positive and negative. The mean SO_2 level was about 34 $\mu g/m^3$; the mean ozone level about 0.4 ppm (although not stated, this is apparently the mean of hourly maxima). Sulfur dioxide was singled out for a detailed analysis of "excess" admissions by disease. Possible lag effects were not mentioned, nor was serial correlation.

Unexpected associations were found for some diagnostic categories: CO was not associated with heart disease admissions; the strongest SO_2 effect was for "infectious diseases," although upper respiratory, bronchitis, and heart disease were also elevated on high SO_2 days. I approximated the relative magnitudes of these effects by estimating elasticities: for this study, a 1% change of air pollution would be associated with a change in admissions of about 0.1% (i.e., $e = 10\%$).

In the second report (*47*), lengths of hospital stays were studied using the same data set. The paper shows that length of stay is also influenced by the day of week of admission, averaging 1–2 days longer for Saturday admissions. Unfortunately, the study emphasized the average pollution levels during the hospital stay rather than the levels preceding it. Perhaps the authors were not aware of the large differences that can exist between indoor and outdoor pollution levels (depending on air exchange rates). Significant (positive) correlations were shown for SO_2, NO_2, and particulates, but in general the values were lower than in the admission data. Significant negative correlations were found for ozone (but not for oxidants). The authors noted that the analysis did not account for the simultaneous effects of temperature and humidity, which also had significant (negative) effects on lengths of stay. In addition, one might expect substantial random variations in lengths of stay because of differences in medical practice.

Interactions and lag effects were examined in the third report (*48*) using multiple regressions and the data set of 223 days from Los Angeles. With respect to admissions, some significant lag effects were shown for relevant diseases, especially for a 3-day lag. The showing for "irrelevant" disorders was similar, except 2-day lags were often significant. No information was presented on correlations between pollutants (which could greatly affect the multiple regression results) or on serial correlation effects. In summary, although the Sterling et al. (*46–48*) studies may have been compromised by neglecting seasonal effects and serial correlation, the facts that temperature was not significant and some of the air pollutants were highly significant ($p < 0.01$) lead to the conclusion that bona fide associations were shown.

A specialized population was studied by Durham (*49*), who used health center records from 1969–1971 from seven California universities to study air pollution-morbidity relationships. This study was notable in several regards: *a*) Air pollution data included daily means and peaks for eight pollutants, collected from within about 5 miles of the campuses where the students resided (patients living more than 5 miles from each campus were excluded from the database). Gravimetrically measured particulates were not included, however. *b*) Both temporal and spatial gradients were analyzed. Two of the universities were in the San Francisco Bay area and five were in the Los Angeles area, which allowed time series to be studied at different overall pollution levels. *c*) Scheduled and repeat visits were excluded from the database. *d*) Data on smoking habits were collected.

Seventy-eight percent of the records showed a physician's diagnosis; gastroenteritis was used as a control diagnosis. To control for day-of-week and other noncausal temporal effects, the dependent variables were coded as the ratios of specific diagnoses to total health center visits for that day (note that this procedure will not account for the possibility that certain diagnoses will be more likely than others to show spurious temporal relationships).

Time lags up to 7 days were studied; analyses were based both on the date of the visit and the date on which the symptom was first noticed. Analyses were performed by university and by calendar quarter. In addition to

correlation analysis, factor analysis was used to combine the effects of weather and air pollution. Correlation results were aggregated by diagnosis for all significant pollutants and by pollutant for all significant respiratory diagnoses.

According to the author (*49*), the results of this study showed that pharyngitis, bronchitis, tonsillitis, common cold, and sore throat in the Los Angeles schools had the highest associations with air pollution. The most important species were peak oxidants and mean SO_2 and NO_2 (all had the same degree of association). Essentially no association was found for the control diagnosis or for particulate matter (as measured by COH). The date that the symptom was first noticed produced better results than the date of first visit, and lags of several days were common. Confounding effects were shown due to the interactions of air pollution with weather changes. Males, nonathletes, and smokers had more respiratory complaints, which were more strongly associated with air pollution. Average pollutant levels in Los Angeles were: oxidants, 0.025 ppm; SO_2, 0.013 ppm; and NO_2, 0.069 ppm. Because few individual pollutant–disease relationships were reported, it is difficult to judge whether any of the positive findings may have been due to chance. Examples of the lag relationships were shown for total respiratory diagnoses and oxidants and SO_2 for one school; approximate elasticities estimated from these results were in the range 7–10%.

A different analytical approach was used by Goldsmith et al. (*50*) in analyzing emergency room visits (all diagnoses) at four Los Angeles hospitals in 1974–1975. Because of the difficulty in separating the pollutant variables, path analysis was used as a means of developing structural equations prescribing the interrelationships among variables representing weather, air pollution, and emergency room visits. This technique depends on prior knowledge of the qualitative interrelationships among the variables; regression techniques are then used to estimate the coefficients defining the quantitative relationship. In this case, the stated intent was to derive relationships between concentrations of sulfur oxides and morbidity. On the basis of bivariate correlations, Goldsmith et al. found significant associations with emergency room visits and temperature and oxidants at all four hospitals, NO_2 and haze at Azusa and Riverside, sulfate at Long Beach and Lennox, SO_2 at Long Beach and Riverside, and CO at Riverside. However, using path analysis, the only remaining significant associations were oxidants at Azusa and sulfates at Long Beach and Lennox. Lag effects were not analyzed in this study, which suggests that the associations might be underestimated somewhat.

Portland, Oregon Study. Jaksch and Stoevener (*9*) studied the daily outpatient "numbers of contacts" with the medical system and their relative costs, during 1969–1970 in the Portland, Oregon standard metropolitan statistical area (SMSA) using records from the Kaiser-Permanente Medical Care Program. Because Kaiser clinics serve only members, the population at risk was known. The analysis was based on a 5% random sample of the membership, but it was not known whether this sample group was representative of the SMSA as a whole. For example, the yearly admission rate was given as 9%, whereas for the Western United States, the expected rate is over 12% (*51*). Use of this sample allowed smoking habits and occupational exposures to be accounted for, and thus the study was an improvement over the usual ecologic design. The air pollution data were limited to TSP samples obtained every fourth day from nine stations. The maximum local annual average TSP was about 70 $\mu g/m^3$; the overall SMSA average was 61 $\mu g/m^3$. The TSP data were interpolated in time using spline fits and geographically to provide values for each patient's home and work address for each day of the 2-year period. Meteorological data consisted of temperature–humidity index (THI).

Diseases were grouped as respiratory (upper and lower), respiratory allergies, other allergies, circulatory, digestive, eye, genitourinary, and other. The dependent variables were the cost per visit and the frequency of visits. Day-of-week effects were not mentioned, except as an index for estimating air pollution exposure. For the cost of respiratory disease visits, air pollution (TSP) was statistically significant for lags of 0 and 1 day, with the best results for the 1-day lag period. Significance levels dropped for 3- and 4-day lags. The correlation coefficient was low (about 0.15), but there were about 1600 (individual) observations. The effect on cost of a 20 $\mu g/m^3$ change in TSP was stated to be quite small, about \$0.03 per medical system contact, which corresponds to a very low elasticity.* The results were qualitatively similar for circulatory and respiratory diseases combined, except that air pollution did not reach significance ($p = 0.4$). Air pollution was not significant with respect to the numbers of visits (nor was any other variable). It should perhaps be noted that Portland has relatively little air pollution and thus it should not be surprising that the air pollution–morbidity effects found were much smaller than for Los Angeles, for example.

Washington, DC. Seskin (*52*) performed a similar study in Washington, DC, for 1973–1974, focusing on a group medical-care practice. Dependent variables were numbers of unscheduled visits to the pediatrics, internal medicine, ophthalmology, and emergency clinics. Respiratory diagnoses were not identified. Air pollutants included oxidants, CO, and SO_2 measured at several different stations. The years 1973 and 1974 were analyzed separately, as was each pollutant-station combination. Missing data were estimated by linear interpolation. Meteorological data consisted of temperature, wind speed, and precipitation. Day-of-week effects were handled by dummy variables for Saturdays and Sundays. No attempts were made to estimate pollutant exposure by combining data from more than one station. Of the 48 regressions (2 years × 3 pollutants × 2 measuring stations × 4 diseases), 8 (17%) were significantly at the 10% level or better (4 oxidants, 2 CO, and 2 SO_2), and 2 (4%) at the 1% level (oxidants and CO with respect to ophthalmology visits). Maximum 1-hr

*For the \$0.03/contact figure to be roughly consistent with the episode of 3–4% per 100 $\mu g/m^3$ mentioned earlier, the average contact value would have to be about \$200–300, which seems unduly high.

values of these pollutants were used in the regression analysis. The magnitudes of the effects shown were in the range 0.5–4.3% change for a 10% change in air pollution (elasticities from 0.05 to 0.43). No consistent lag effects were found. In view of the poorly characterized exposures, the "true" effects (if any) could have been longer, although this source of underestimation could have been balanced by the failure to consider serial correlation. Weather effects were minimal compared to the day-of-week effect.

Chicago Studies. Emergency room admissions data from the Cook County Hospital from September 1971 to March 1973 were analyzed by Carnow (*53*), Namekata and Carnow (*54*), and Fishelson and Graves (*55*).

Carnow (*53*) used deviations from moving averages as a means of seasonal adjustment and presented results of stepwise regression analysis for emergency room admissions on Tuesdays during the two winters of the study period ($n = 30$). Diagnostic groups studied were asthma, acute bronchitis, pneumonia, total respiratory, heart attacks, congestive heart failure, and total cardiac diagnoses. Air pollutants were SO_2, COH, and CO, based on an eight-station monitoring network. Exposure data were computed by weighting the monitoring data to reflect proximity of the patients' home addresses to the various stations. Weather variables were also included in the regression procedure, giving a total of 12 independent variables that could be selected. The results showed significant associations between SO_2 and respiratory admissions and between CO and congestive heart failure admissions. There were no significant associations with COH. The absolute magnitude of the effects appeared to be small; assuming that the regression coefficients are given as daily admissions per ppm, the largest seasonally adjusted SO_2 deviation was associated with an increase in total respiratory admissions of less than 1%.

Fishelson and Graves (*55*) considered SO_2 and COH averaged from five monitoring stations near the hospital, in addition to temperature, relative humidity, and sky cover. Mean values for SO_2 and COH were about 60 and 88 $\mu g/m^3$, respectively. The paper is not explicit but implies that 24-hr averages were used for the air quality data. The data set consisted of emergency room visits on 81 Tuesdays broken out by age, sex, race, and cause. Dummy variables were used to account for holidays. Both linear and logarithmic models were examined, including lags up to 3 days. Serial correlation was considered by means of the Durbin-Watson statistic. In addition, some regressions incorporated a lagged dependent variable as an explanatory (independent) variable to "capture various effects prevailing in the study area that could change over time and affect admissions." Using this variable increased the R^2 values. In general, the linear regression results associated cardiac admissions with SO_2, with a 1-day lag ($p = 0.005$). For most of the significant regressions, the Durbin-Watson test was either inconclusive or indicated no autocorrelation. Males and females participated about equally in the cardiac–SO_2 relationship, but when grouped by age, only the over-59 group was not important. By implication, the age groups 5–40 must have also been important (results not shown). However, when the regression included the total of same-day and lagged pollution and the lagged dependent variable, all the age groups over 1 year were significant. COH was significant (positive) only for cardiac admissions in the 40–59 age group. Respiratory admissions were only significant for the over-59 age group for lagged SO_2.

For a regression using logarithmic transforms for dependent and independent variables, the elasticity is numerically equal to the regression coefficient. These elasticity values seem unduly large in comparison to the studies reviewed above, with many values around unity and higher, for example. Fishelson and Graves did not include a table of mean values in their paper, but the pertinent values may be obtained from Krumm and Graves (*56*) (discussed below); the resulting linear model elasticity estimates are an order of magnitude lower than the log models (placing them more in line with the other studies), which suggests large differences between linear and logarithmic specifications. Also, in their calculations of the potential benefit of reducing ambient SO_2 in Chicago, they apparently erred by not considering that the regressions using the total of same-day and lagged SO_2 produce regression coefficients one-half the size of those using single-day figures.

Krumm and Graves (*56*) reanalyzed this data set (but did not refer to the first paper), emphasizing total respiratory plus cardiac admissions and including interactions and higher-order terms for the pollutants. In their ordinary least-squares regression using logarithms, SO_2 was not significant (negative) and COH was significant and positive. In subsequent regressions, the interaction term $SO_2 \times$ COH became significant. This paper emphasized theory and presented few useful new results. This data set yielded very different findings depending on which of three different methodologies was used and is thus mainly of theoretical interest.

Namekata et al. (*57*) studied admissions to two Chicago hospitals (including Cook County) for Tuesdays, Wednesdays, and Thursdays, for 1 year beginning April 1977. They included patients age 15 or older for five disease groups: all respiratory diagnoses; allergic conditions and upper respiratory infections; acute bronchial and lower respiratory infections; all cardiac diagnoses, and hypertension and vascular heart disease. Weather data (temperature, wind speed, precipitation, relative humidity, hours of possible sunshine, and sky cover) were from Midway Airport. Daily community exposure estimates were made for 76 residential areas for three pollutants (TSP, SO_2, and NO_2) based on an interpolation procedure using routine monitoring network data. Only days with reasonably complete records were retained in the study (20 days for SO_2 and NO_2; 42 for TSP; 131 when a single hospital and monitoring station were used [CO and NO were added]; 36 days for ozone in the summer).

Regressions were run with one pollutant at a time. For total respiratory diagnoses, only NO was significant, although SO_2 was close ($p = 0.15$) for the small data set. For allergic conditions and upper respiratory infections, only NO approached significance ($p = 0.10$). For acute bronchial and lower respiratory infections, SO_2 was signif-

icant in both data sets, but negative in the larger one. For cardiac diagnoses, SO_2 was significant ($p<0.05$, $n=20$); NO, and NO_2 were close ($p<0.10$). For hypertension and vascular heart disease, ozone was significant (negative) and NO was close. The SO_2 elasticities were about 50% for total respiratory diagnoses and about 400% for cardiac conditions (this extraordinarily high value suggests collinearity problems). Serial correlation was not examined in this study, but since it was not a complete time-series (due to missing data), this problem may be less important. Lag effects were not mentioned, presumably for the same reason.

Steubenville, Ohio. Samet et al. (*58*) analyzed emergency room visits in the industrial city of Steubenville, Ohio, for the months of March, April, October, and November during 1974–1977. They used deviations from the expected numbers of admissions based on day of week, season, and year as the dependent variable, for all respiratory diseases, all diseases except trauma, and all diseases. Air pollution variables were 24-hr averages from a nearby station for SO_2 (mean = 90 $\mu g/m^3$), TSP (mean = 156 $\mu g/m^3$), NO_2, CO, and ozone. Deviation variables were not used for the pollutants because the authors noted no weekly cycles or long-term trends, based on inspection. The correlation between SO_2 and TSP was 0.69; all other pairwise pollutant correlations were lower.

Results were presented in terms of quartile analyses for two subsets stratified by ambient temperature. Dose–response relationships were not clearly evident from these data. Linear regressions found that either (unlagged) SO_2 or TSP was associated with respiratory disease visits ($p<0.05$); TSP was also associated with trauma (J. M. Samet, personal communication) and all diseases. The elasticities for respiratory visits were about 4.5%; for all diseases they were about 2%. The regression coefficients for respiratory diseases were about 3% per 100 $\mu g/m^3$ for smoke and 5% per $\mu g/m^3$ for SO_2, which are consistent with previous figures. In no case did a lagged variable provide a better fit. The possibility of serial correlation was mentioned, but no data were given.

Pittsburgh. Mortality and morbidity from 1972–1977 were studied in Allegheny County, Pennsylvania, by Mazumdar and Sussman (*59*). The morbidity variables were "daily numbers of emergency and urgent hospital admissions" from all acute care hospitals in the county, for all causes, respiratory diseases, heart disease, and other circulatory disease. Respiratory diseases constituted about 8% of the total urgent and emergency admissions (rate = 6.7/1000 population). The data were analyzed as deviations from 15-day moving averages, corrected for temperature variation, and adjusted for day-of-week effects. Results were given in terms of the percentage of that morbidity measure attributable to a given pollutant. Sulfur dioxide and smoke, measured at three different locations, were the pollution variables, with means of about 94 and 100 $\mu g/m^3$, respectively; results were presented for each pollutant separately and for both jointly. Significant results were obtained for smoke separately in 7 out of 12 regressions, with the pollution effects ranging from 0.9% for all causes to 4.4% for heart disease. As a separate pollutant, SO_2 was significant in 3 of the 12 cases, but 1 of these was negative. Sulfur dioxide was never significant in the joint regressions; the results for smoke were not greatly different than in the separate regressions. There was essentially no relationship between the results for morbidity and mortality variables; the morbidity results were larger in magnitude and more statistically significant.

Carbon Monoxide Effects in Denver. Kurt et al. (*60,61*) studied cardiorespiratory complaints (CRC) presented to a Denver, Colorado, hospital emergency room over a 3-month winter period in 1975-1976, in relation to CO concentrations and other air pollutants. Carbon monoxide was emphasized in part because it is thought to be a particular problem in Denver because of the high altitude and traffic density there. The two presentations of this study (*60,61*) differ only in the statistical analysis techniques used. Carbon monoxide data were obtained from a monitoring station located 300 m from the hospital; data on ozone, NO_2, and SO_2 were also obtained from this station. The 24-hr mean CO levels showed a better correlation with CRC than did daily peaks. The average daily maximum CO concentration was 32 ppm on the 24 highest CO days (Fig. 10). No corrections were made for weather variables or for seasonal or weekly cycles; the scatter plots shown suggested that weekly cycles may have been present. Carbon monoxide was positively correlated with temperature; no information was given on the effect that this may have had on the CRC–CO relationship. No control analyses were presented, either for other symptoms versus CO or for CRC versus other pollutants, although the authors reported that the other pollutants showed no consistent relationships with CRC trends.

Linear correlations between CRC and CO were not significant on a same-day basis; neither were the grouped mean data shown in Figure 10. However, the relationship strengthened when a 1-day lag was considered (*60*). Significant differences in CRC were found when these 2-day periods were grouped according to high and low CO

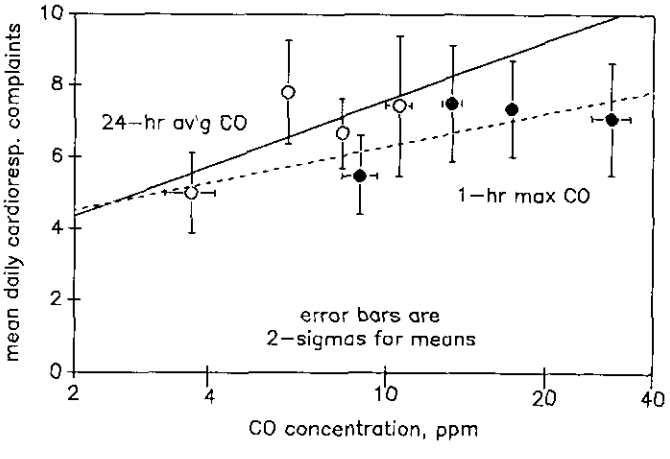


FIGURE 10. Dose–response functions for cardiorespiratory complaints at a Denver emergency room. Data from Kurt et al. (*61*).

concentrations. The grouped mean data (*61*) shown in Figure 10 show the following tendencies in the data: a nonlinear dose–response relationship (the X-axis is logarithmic), a CRC intercept of three to four complaints per day, a more consistent relationship when 24-hr mean CO is used as the dose metric, and elasticities of about 0.4–0.5. The elasticities are lower if a linear CO variable is used.

Considering the typical spotty spatial distributions of CO and hence the likely errors in population exposure (only one monitoring station was used and its proximity to the hospital is not relevant to population exposures before admission), this study must be judged as showing an important relationship between air pollution and cardiorespiratory health. It is unfortunate that other pollutants were not given the same level of detailed analysis or that "control" diagnoses were not examined.

Utah. A period of heavy smog conditions in the Salt Lake Valley was studied by Lutz (*62*) in relation to patient visits to a family practice clinic in Salt Lake City. The analysis was based on 13 weekly totals of patients with pollution-related diseases, as a percentage of the total number of patients for that week. Pollution-related diseases were asthma, cough, dyspnea, acute bronchitis and bronchiolitis, pneumonia, emphysema or chronic lung disease, acute upper respiratory tract infection, laryngitis, sinusitis, conjunctivitis, ischemic heart disease. Only 2% of the patients had heart-related complaints. Air pollutants considered included particulates (TSP), CO, ozone; weather variables were percentages of cloud cover and of days with smoke or fog. The author thought that some portion of SO_x effects would be embodied in the TSP variable. Only bivariate correlations were performed; the most highly correlated variables were particulates and percentage of smoke/fog ($p < 0.005$). Ozone was significantly negatively correlated with the percentage of patients with pollution-related diseases; this finding was ascribed to collinearity with cloud cover (negative). However, temperature was not considered in this study and could thus be a confounding variable.

In a brief reanalysis of these data, I added daily minimum and maximum temperature data obtained from the *World Weather Disc* (*63*) for Salt Lake City, averaged to provide weekly data corresponding to the pollution and patient data (daily temperatures from Ogden were quite similar). I converted the pollutants standards index (PSI) data used by Lutz to TSP by setting TSP = 260 $\mu g/m^3$ at a PSI value of 100. In a multiple regression, both (maximum) temperature and TSP were significantly associated with the percentage of pollution-related outpatient visits. These relationships are displayed here in two different ways. Figure 11*A* shows the relationship with TSP as the sole predictor and adjusted to a constant temperature of 42°F based on the regression coefficient; the overall trend is not greatly affected by the adjustment. However, as seen in Figure 11*B*, if temperature is considered to be the primary predictor, only 5 weeks stand out as different from the rest of the data; these 5 weeks consisted of five of the six highest TSP values. These 5 weeks were not consecutive, which rules out an infectious epidemic as the source of the increased prevalence of pollution-related visits. The maximum point was week 7, just before Christmas. Deleting the observation had little effect on the regression slope, which was about 12% per 100 $\mu g/m^3$. Although this study was brief and simple (and did not use a control), it does not suffer from day-of-week or lag effects, and the use of percentages rather than the absolute numbers of visits

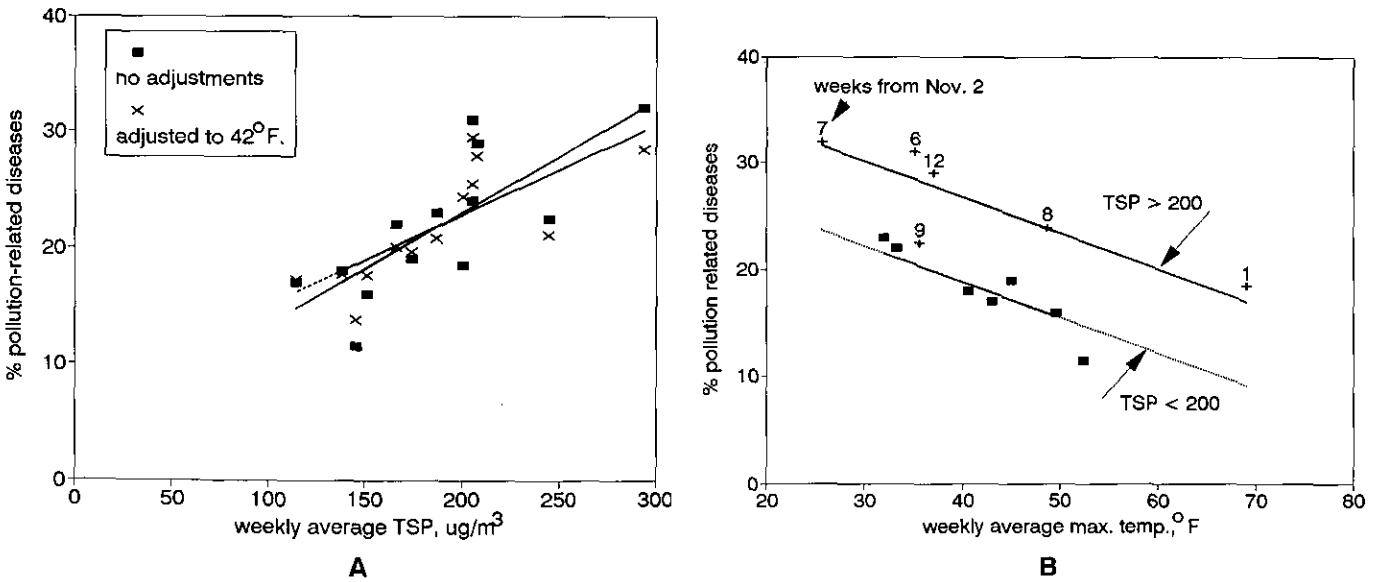


FIGURE 11. Relationships between visits to a family practice clinic for pollution-related diseases in Salt Lake City and environmental factors, based on data from Lutz (*62*). (*A*) Based on total suspended particulates (TSP), after adjustment for temperature, (*B*) based on temperature, showing weeks of high TSP.

helps account for seasonality. The regression slope (the elasticity was about 70%) was substantially higher than found in previous studies of hospital admissions based on daily data. Explanations could include the use of a less severe measure of morbidity (clinic visits versus hospital admissions) or the use of weekly data, which effectively adds the lag effects. The multiple regression would predict about 11% pollution-related diseases for a summer week in which TSP averaged 50 $\mu g/m^3$ and the maximum temperature was 80°F, which does not seem unreasonable (although it is outside the range of the data).

Pope (*64*) analyzed inpatient hospital admissions in Utah County (Provo, Utah and vicinity) during a period that included the shutdown of a nearby steel mill, which was a major source of air pollution including particulates and presumably sulfur oxides. The observations consisted of 35 monthly averages of inhalable particle concentrations (PM_{10})* and inpatient hospital admission statistics, beginning April 1985. The plant was shut down from August 1986 to September 1987, during which time period PM_{10} levels were noticeably lower than corresponding previous months, especially in December and January. In winter, this region suffers from air stagnations due to inversions, which tend to increase concentration levels of all air pollutants. For example, the 1984 maximum 24-hr TSP reading reported by EPA at this location was 412 $\mu g/m^3$, which is well above the U.S. ambient standard (260 $\mu g/m^3$).

The categories of hospital admissions considered were diagnoses of bronchitis or asthma (mean = 1.5/1000 population), pneumonia or pleurisy (mean = 1.75/1000), and the sum of these two groupings. The average hospitalization rates in Utah County were substantially lower than comparable values for the United States, on the basis of Census Regions. The lower rates in Utah may be due to lower rates of smoking and/or a younger population. Pope stratified the population into adults and children younger than 18.

Pope recognized that his analysis was compromised by the coincidence of peak air pollution periods with the normal winter peak in respiratory disease and used ambient temperature (monthly mean of daily lows) as a control variable. Control population groups included all nonrespiratory admissions and admissions for out-of-country residents. Regression results were presented using the current month and the previous month (i.e., a lag of 30 days), for PM_{10} alone and with temperature. Temperature was significant in 7 of 10 regressions, including the control groups. Including temperature reduced the PM_{10} regression coefficients for respiratory admissions, but Pope found PM_{10} to be a significant predictor of all categories of respiratory admissions for children, of bronchitis/asthma admissions for adults, and for the combined category of all respiratory admissions. Values of R^2 ranged up to 0.83 (the high value of explained variance results in part from the use of monthly rather than daily data). Use of a lagged variable usually increased the correlation. In general, the particulate regression coefficients were much larger than found by previous authors. For example, Pope's results imply an approximate doubling of children's admissions and a 25% increase in total respiratory admissions in response to an increase of about 90 $\mu g/m^3$. On the basis of equivalent TSP, this corresponds to about 16% per 100 $\mu g/m^3$. This large response was attributed by Pope to the high percentage of nonsmokers (95%) in the study population; an additional possibility is the use of monthly averages. In addition, as discussed above, when both lagged and unlagged variables included in a multiple regression and autocorrelation exists, the true effect of the parameter is the sum over all the lags.

Because of these interesting findings, I reanalyzed this data set, using data values read from the graphs in the paper. Because temperature data were not presented, I used a seasonal correction factor consisting of periodic functions peaking in January or February with corresponding minima in July or August. As a first check on Pope's findings, I compared the 13-month means for the period of plant shutdown with a similar 13-month mean previous to the shutdown. This gave a 12.5% difference in total admissions, due almost totally to children's admissions. Regression coefficients computed on this basis were consistent with Pope's results, which included the temperature covariates. Next, a two-stage adjustment procedure was used, in which admissions were first adjusted for seasonal effects using the periodic function and then regressed against PM_{10}. This procedure minimizes any pollution effects that have a seasonal pattern similar to the admissions data because all of the (average) seasonal effect is removed by adjustment. However, PM_{10} remained significant for both children's and total respiratory admissions. These results are plotted in Figure 12. Finally, the high-pollution months of December, January, and February were removed from the data set, and admissions were regressed against PM_{10} without seasonal corrections; results were significant for total and adult admissions. Regressions using the periodic function and PM_{10} gave results similar to Pope's. A dummy variable representing the plant's operating condition was never significant when used in conjunction with PM_{10}, implying negligible effects associated with any other emissions from the plant not in phase with PM_{10}. (In a personal communication, Pope indicated that coke ovens are largely responsible for the steel plant's emissions, which suggests a complex mixture of air pollutants including SO_2. He also expressed the opinion that the PM_{10} particles are mainly sulfates and nitrates during winter inversion conditions, which are often quite foggy. Thus, assigning the association of hospital admissions to PM_{10} alone may be misleading.)

My reanalysis thus essentially verified Pope's conclusions, but some interesting questions remain that could probably best be explained by an analysis of daily (or perhaps weekly) values: Is the 30-day lag effect real or an

*PM_{10} refers to particles collected using a sampler designed to exclude particles with an aerodynamics diameter greater than about 10 μm, sometimes referred to as thoracic particles. In practice, 60–80% of the particle diameters will be less than 10 μm (F. McElroy, U.S. Environmental Protection Agency, personal communication, March 15, 1991).

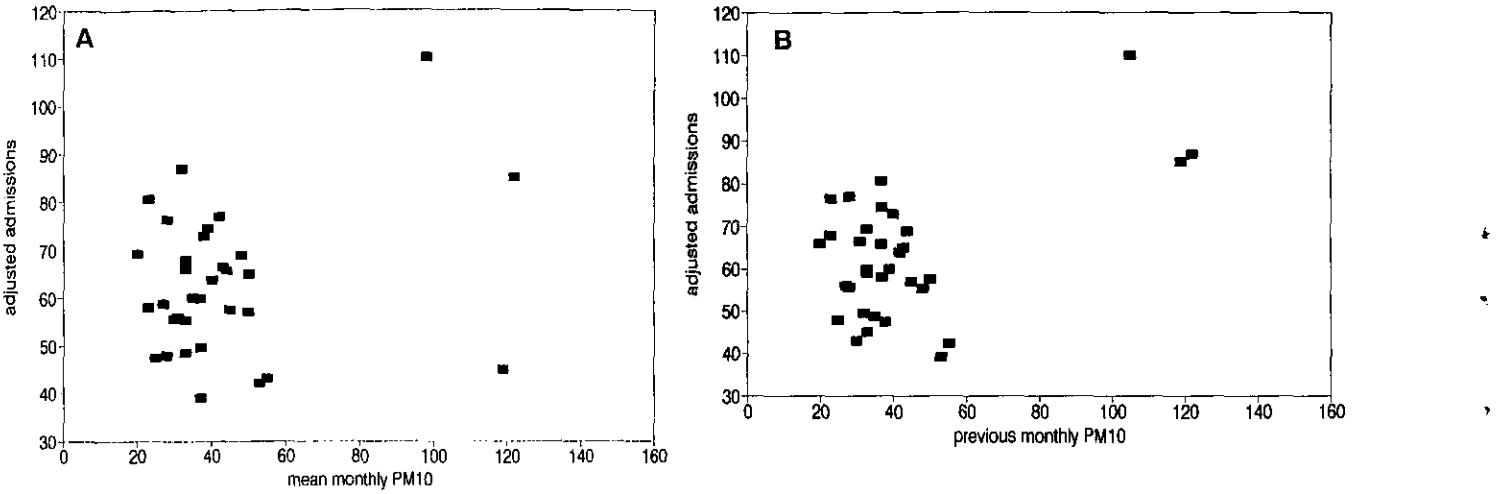


FIGURE 12. Dose–response data for hospital admissions in Utah County, UT, after adjustment for seasonality. (*A*) Based on PM_{10} for the same month, (*B*) based on PM_{10} from the previous month. *Data from Pope (64).*

artifact of the analysis? Are there effects due to any other pollutants? Are there associations with any other admissions diagnoses?

Pope extended his analysis to 1989 (*65*) and included two additional geographic areas. Salt Lake Valley, which includes Salt Lake City and County and the southern portion of Davis County, was intended to provide additional cases, while Cache County was intended as a control. Cache County includes the city of Logan and is located more than 100 km north of the other two areas. Populations were demographically similar in all three areas, but Cache County had fewer people and lower particulate levels (and also less complete air monitoring). The age categories were changed for the second paper, consisting of all ages and preschool-age children, and ICD-9 codes were used instead of diagnosis-related groups. In general, the results of the extended analysis were similar to those of the first paper. The coincidence of peaks in hospital admissions and PM_{10} was less pronounced in 1989, so that overall regression coefficients were reduced somewhat. PM_{10} was a significant predictor of hospitalization in Salt Lake Valley but not in Cache County, as expected, as the PM_{10} data used in the Cache County regressions were measured in Utah County. This verifies that the PM_{10} variable was not serving as some sort of surrogate seasonal indicator, independent of local pollution levels.

The paper by Lamm et al. (*66*) was intended to refute Pope's (*64*) earlier claim that particulate air pollution was the major factor in children's hospitalization in Utah County. Lamm's approach introduced data on viral activity as an additional explanatory variable and appears to be the first to consider both infectious agents and environmental factors simultaneously. Such an approach is consistent with a model in which air pollution exacerbates rather than causes disease. The infectious agent in question, respiratory syncytial virus (RSV), occurs with great regularity in all climates in winter or early spring, is particularly important in urban areas, and results in hospitalization of young children (*10*). RSV can also affect adults, but the response is usually milder than in young children (*67*).

A variable such as RSV prevalence describes the fundamental cause of illness and would be expected to have a 1:1 diagnostic relationship with the appropriate diseases, just as all patients having the flu exhibit one or more strains of influenza virus. The question of relevance here is, given the presence of an infectious agent, do environmental factors exacerbate its effects? The high degree of collinearity between RSV and PM_{10} in Utah make it difficult to answer this question with confidence.

Lamm et al. (*66*) considered Utah and Salt Lake Counties separately, but used a regional surrogate to represent the monthly trends in RSV activity. RSV is the major cause of bronchiolitis in young children and was used by Lamm et al. to represent RSV activity throughout the area. The paper shows a reasonably close relationship (graphically; no correlation was reported) between the total RSV laboratory analysis for six states and the sum of bronchiolitis admissions in both counties. This admissions variable was then labeled "RSV clinical activity" for use in the regression analysis. It is noteworthy that when Lamm et al. regressed bronchiolitis admissions in Utah County against this variable, current and lagged PM_{10} variables, and a lagged temperature variable, PM_{10} remained significant ($p < 0.02$ for the sum of lags), indicating the importance of local envionmental conditions in addition to the regional level of infection. Lamm et al. concluded that "PM_{10} showed no consistent significant association with hospitalizations for any of the pediatric lower-respiratory tract diseases. In total, RSV is the single determinant examined that reconciles the patterns of hospitalizations for various pediatric diseases of the lower respiratory tract seen in Utah and Salt Lake Counties (1985–1989)" (*66*).

However, a careful reading of Lamm et al.'s results would take issue with assigning excess hospitalization solely to RSV. They state that only 2 of 36 regression

coefficients other than RSV were significant at the 0.05 level (as would be expected due to chance alone), whereas the tables actually show three such values, and a fourth one narrowly misses the mark. The 36 regression possibilities for children include 12 temperature coefficients; because of the strong seasonal dependence, we would expect RSV to primarily displace temperature. Adding a variable with no expected significance to the pool of possibilities always tilts the comparison toward the null hypothesis. If we combine the lagged and same-day PM_{10} variables as discussed above, there are 12 possibilities, three of which are significant at the 0.05 level. Further, there are several individual PM_{10} coefficients that just miss the 0.05 level; six values out of 24 were significant at the 0.15 level, for example. For adults, RSV was not significant and one of the six summed PM_{10} coefficients reached the 0.05 level. Lamm et al. (*66*) performed no regressions of combined age and diagnosis categories that could be compared with Pope's results (which were significant for PM_{10}). While this statistical performance is certainly not robust, neither does it warrant Lamm et al.'s conclusion to totally discount the role of air pollution. The appropriate conclusion would appear to be that air pollution contributes to the exacerbation of respiratory disease that is primarily caused by biological agents. If the significant coefficients reported by Lamm for Utah County are used to estimate the hospital admissions attributable to PM_{10}, the fraction of total pediatric admissions comes to about 15%, which is reasonably consistent with the elasticity estimates from other studies.

Canadian Studies. Levy et al. (*68,69*) analyzed weekly hospital admissions due to acute respiratory causes (bronchitis, bronchiolitis, emphysema, pneumonia, asthma) in Hamilton, Ontario, from July 1970 to July 1971. The authors reported that only patients with recent histories (< 5 days) of acute respiratory complaints were included. Most of the analysis was based on SO_2 and haze and a combined air pollution index (API), using data from a central monitoring station; no significant correlations were found for oxidants or CO. The correlations appeared to be better for API ($p < 0.001$) than for either of its constituents alone. The correlations diminished for hospitals more distant from the monitor, suggesting the influence of local as opposed to regional air pollutants. No seasonal corrections were made (although a seasonal effect was apparent from the scatter plots given), but in a combined regression with temperature, air pollution remained significant ($p < 0.001$). Bivariate correlations suggested that SO_2 may have been slightly more significant than haze, but in the absence of seasonal adjustments, this conclusion would be speculative.

Using the weekly data read from a graph (*68*), I reanalyzed the relationship between respiratory admission and API, including a linear variable for the secular trend and a periodic function to represent the seasonal cycle. Neither of these variables was significant, and including them reduced the API regression coefficient only slightly. The relationship is shown in Figure 13 (data are segregated by season) and is an order of magnitude stronger than the typical results from daily time-series

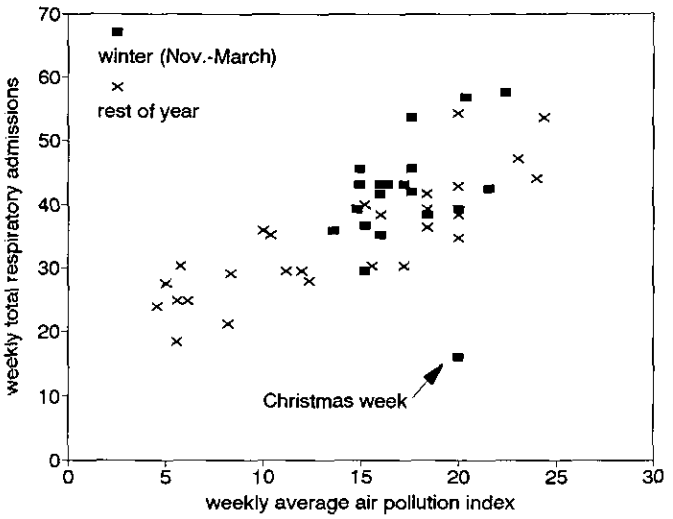


FIGURE 13. Dose-response relationship for respiratory admissions in Hamilton, Ontario, 1970–1971. Data from Levy et al. (*69*).

analyses. Part of the difference may lie in neglecting weather effects, and part may be due to the use of weekly data, which in effect aggregates all the daily lags. As a further check on these differences, I aggregated the data into monthly periods and repeated the regression analysis. The slope dropped about 30%, but the R^2 remained about the same. One could interpret the difference between the weekly and the monthly slopes as the short-term response; this estimated value agreed well with the results from studies of daily fluctuations in other studies. Whether the long-term component is an artifact of the analysis or a bona fide response to air pollution cannot be answered with these data.

Bates and Sizto studied temporal variations in admissions to a group of acute care hospitals in Southern Ontario (*8,70–73*). These papers should be considered as a group because the details and limitations of the methodology become more apparent in the later works. Bates et al. (*74*) used similar methods to study hospital emergency room visits in Vancouver.

The Ontario studies involved a population of about 5.7 million people (1977–1978 figures) in an area of about 64,500 km^2; the Sudbury area (known for its very large SO_2 source) was not included. Data from 79 hospitals and 15 air monitoring stations were pooled in these analyses, which were limited to the bimonthly periods of January–February and July–August. Weather data consisted of daily mean temperatures, averaged for two stations; air quality data for the first study consisted of daily maximum readings of SO_2, ozone, NO_2, and soiling index (COH) for 0-, 24-, and 48-hr lags. In the later papers (*70–73*), Bates added sulfate aerosol and relative humidity to the data set (and more air sampling stations) and extended the analysis to 1980, 1982, and 1983, respectively. The data pooling technique used was to sum the admissions over all hospitals and to average the air quality data from all included monitoring stations having a reading for the day in ques-

tion. In the case of sulfate aerosol, most stations recorded (24-hr averages) only every sixth day on a rotating schedule, so that only a few stations were averaged each day. However, some of the sulfate stations recorded data every day or every third day, a point that seems to have been overlooked by Bates and which could contribute some inadvertent geographic weighting to the averages. Bates selected as his air quality stations those that measured all the pollutants at the same location.

Diagnoses studied included all causes, nine different respiratory diagnoses, and several nonrespiratory (control) causes. Cardiac diagnoses were not studied. Total admissions averaged about 2300 per day, total daily respiratory admission about 40 in summer and 70 in winter, asthma about 18/day in winter and 16/day in summer, and the nonrespiratory causes (*8*) were about 20 per day. The respiratory admissions studied did not include most upper respiratory causes nor problems with tonsils or adenoids, which accounts for the lower annual average admission rate compared to the U.S. figures given previously for all respiratory causes (3.4/1000 population or about 2.3% of all admissions versus 13/1000). The dependent variables used in the time-series analyses were the deviations from the averages for each day of the week and season. In the latter two papers, deviations were also normalized for each year to remove any spurious correlations that might have resulted from long-term trends in the data. Such "detrending" was not performed within the 2-month seasons, however. Deviation variables were not used for the pollutants; the authors cite the lack of a weekly pattern in ozone as justification.

Over the 9-year study by Bates and Sizto (*8,70–73*), there were substantial changes in the air quality and in hospital admissions, which they did not specifically consider. Because long-term hospitalization trends may have other causes, such as changes in medical or insurance practices, it may be useful to examine these long-term temporal trends for consistency with the daily deviation associations found by the formal time-series analyses. Figure 14 shows the air-quality trends plotted on a logarithmic scale, so that percentage changes may be compared directly at any concentration level. Sulfur dioxide shows a substantial decline in both summer (July–August) and winter (January–February) periods, sulfate peaks in the middle of the period, and the remaining pollutants show no particular trends. Figure 15 shows the relative changes in hospital admissions over this time period, by dividing the annual admissions by the 9-year mean. Total admissions (all diagnoses; Figure 15*A*), show a more-or-less continuous decline over time, with the exception of the winter of 1983 (possible flu epidemic?). Respiratory admissions are more variable from year to year. Asthma admissions are compared to the remaining respiratory categories in Figure 15*B*; the increase in asthma admissions (discussed in general below) is seen to be confined to winter. Note that Bates and Sizto adjusted the asthma admissions figures after 1979 to account for the change in ICD-9 coding.

Bates and Sizto (*8,70–73*) used bivariate correlation coefficients as measures of association, in addition to selected multiple regressions. Table 1 presents a comparison of the bivariate correlations from the four papers (*8,70–72*), for winter and summer periods, respectively. The tables show the maximum (absolute values of R) correlations for any of the three lag periods for the four papers, listed in chronological order. In comparing across studies, one should keep in mind that the long-term relationships have not been removed from the first two papers. These entries confirm the trends shown in Figures 14 and 15. Bates and Sizto listed all the correlations in the first paper, regardless of significance level; only significant values ($p < 0.01$) were listed in subsequent papers. Thus, blanks in Table 1 represent correlations that did not achieve the 1% level.

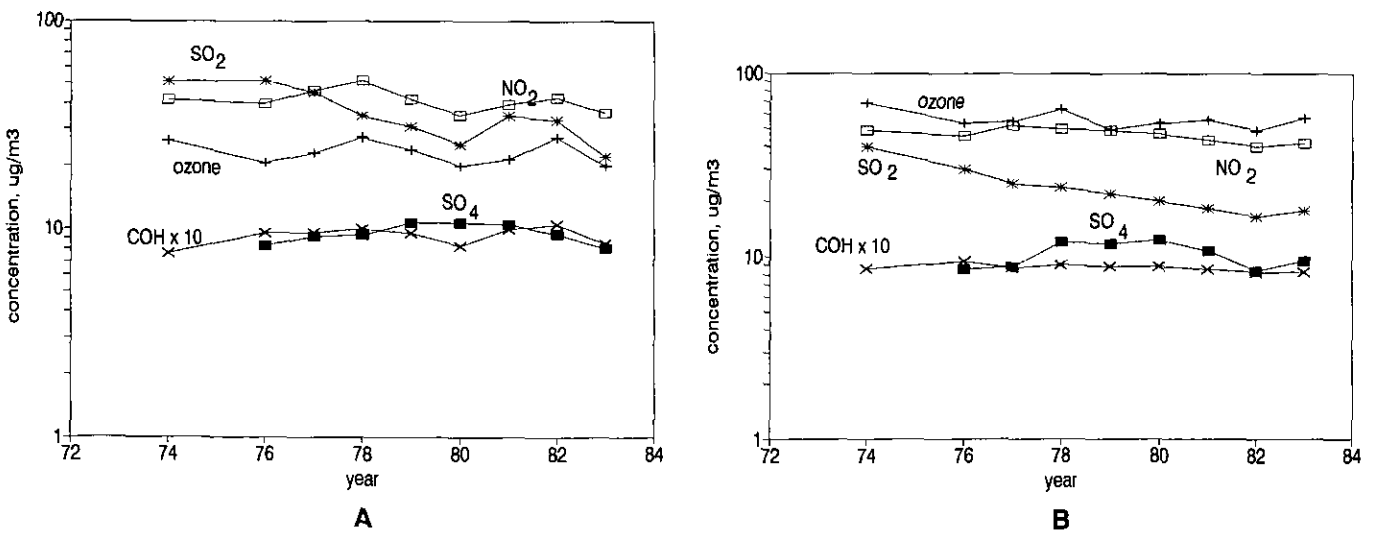


FIGURE 14. Long-term trends in air quality in Southern Ontario. (*A*) January–February, (*B*) July–August. Data from Bates and Sizto (*8,72*).

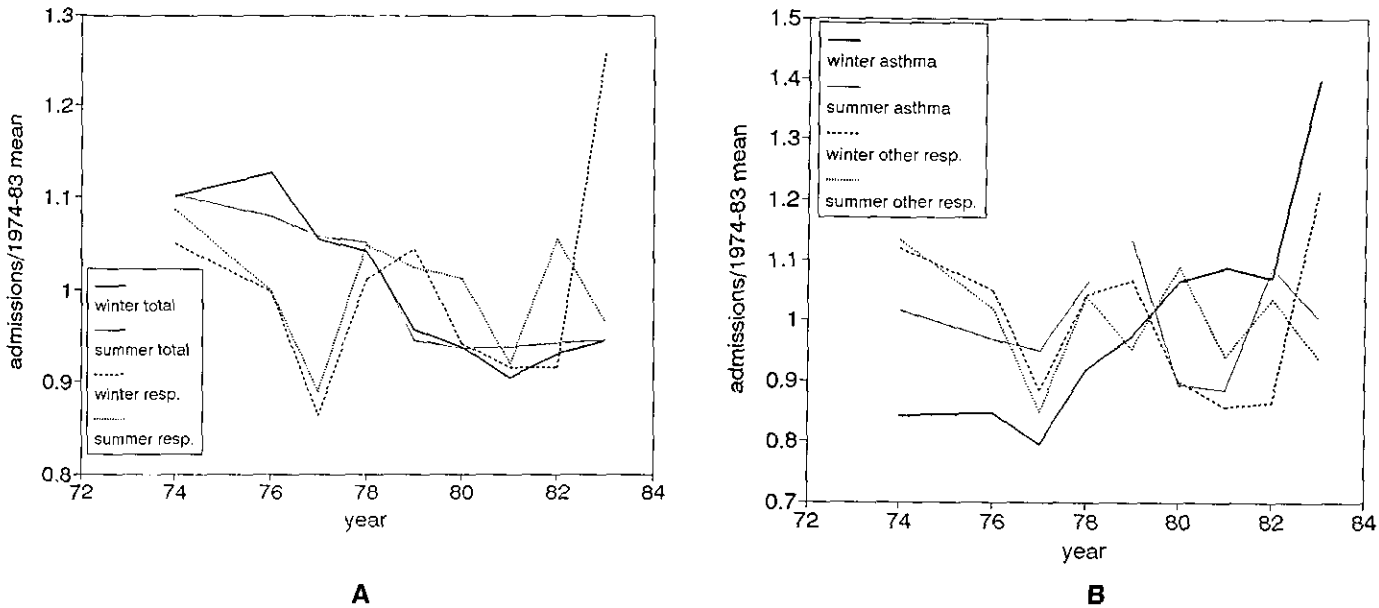


FIGURE 15. Long-term trends in hospital admissions in Southern Ontario. (*A*) Total admissions (all diagnoses), (*B*) asthma and other respiratory admissions. Data from Bates and Sizto (*8,72*).

Table 1. Comparison of hospital admissions studies by Bates and colleagues.[a]

		Diagnostic category					
Pollutant	Source	Total	Respiratory	Respiratory–asthma	Asthma, all ages	Asthma, 0–14 years	Nonrespiratory
January–February correlation coefficients							
SO_2	1	0.230	(0.060)[c]	NA	(−0.090)	(0.030)	− 0.160
	2	0.416		0.171	− 0.282	− 0.248	
	3						
	4						
NO_2	1	−0.310	(−0.060)	NA	0.130	(0.090)	(0.110)
	2	0.159			− 0.215	− 0.238	
	3	0.112				− 0.117	
	4					− 0.117	
Coefficient of haze	1	−0.140	(0.100)	NA	(0.080)	(0.090)	(0.070)
	2						
	3	0.134					
	4	0.127					
Ozone	1	−0.230		NA	0.120	(0.080)	(0.060)
	2				− 0.146	− 0.182	
	3						
	4						
SO_4^{2-}	1	NA	NA	NA	NA	NA	NA
	2	−0.259			0.156	0.174	
	3						
	4						
Temperature	1	0.240	0.280	NA	0.140	(0.070)	(−0.050)
	2	0.212	0.196	0.149			
	3		0.120		0.186	0.211	0.179
	4		0.120		0.171	0.194	0.150
Relative humidity	1	NA	NA	NA	NA	NA	NA
	2						
	3					0.113	
	4						

(continued)

Table 1. *Continued.*

Pollutant	Source	Diagnostic category: Total	Respiratory	Respiratory–asthma	Asthma, all ages	Asthma, 0–14 years	Nonrespiratory
July–August correlation coefficients							
SO_2	1	0.160	0.290		0.170	0.140	(0.100)
	2	0.279	0.207	0.239			
	3		0.147	0.117	0.118		
	4		0.138	0.112	0.106		
NO_2	1	0.050	(0.120)		(0.110)	(0.090)	(0.080)
	2		0.128				
	3	0.118	0.123				
	4	0.114	0.110			− 0.117	
Coefficient of haze	1	(0.110)	(0.080)		(0.050)	(0.060)	(0.040)
	2						
	3	0.156					
	4	0.159					
Ozone	1	0.160	0.280		0.210	0.140	(0.090)
	2	0.218	0.223	0.217	0.124		− 0.236
	3	0.132	0.166	0.154			
	4	0.122	0.147	0.149	0.124		
SO_4^{2-}	1						
	2		0.264	0.186	0.212	0.196	− 0.261
	3		0.180	0.129	0.147		
	4		0.171	0.134	0.127		
Temperature	1	0.210	0.230		(0.120)	(0.070)	(0.080)
	2		0.148	0.151			− 0.355
	3	0.129	0.141	0.189			
	4	0.108	0.129	0.168			
Relative humidity	1	NA	NA	NA	NA	NA	NA
	2						
	3						
	4						

[a]Largest (absolute) r values for any lag period are shown in table. Blank areas in table indicate that data were not provided in original reference. NA, not applicable.

[b]Source: 1, Bates and Sizto, 1983 (*8*). Data from 1974, 1976, 1977, 1978; 2, Bates, 1985 (*70*). Data from 1974, 1976–1980; 3, Bates and Sizto, 1986 (*71*). Data from 1974, 1976–1982, detrended; 4, Bates and Sizto, 1987 (*72*). Data from 1974, 1976–1983, detrended.

[c]Numbers in parentheses denote $p > 0.05$. All other entries are significant.

In the winter period (Table 1), admissions for all diagnoses were significantly correlated with SO_2 and temperature and negatively with ozone, NO_2, and sulfate. However, these relationships did not survive the detrending process and thus must have been associated mainly with long-term variability. Total admissions were correlated with COH in the latter two (detrended) studies. Admissions for all respiratory diagnoses were significantly correlated with temperature for all four studies (note the reduced values for the detrended studies), as were asthma admissions in three of the four. No pollutant variables were consistently associated with any of the respiratory diagnosis admissions categories in winter. Correlations for the nonrespiratory or control admissions were mostly nonsignificant, except for temperature.

There were many more significant correlations in the summer period (Table 1), except for relative humidity, roughly 40% of the 151 possibilities, at the 0.01 significance level or better. For total (all diagnoses) admissions, COH was significant, as in winter, and had the highest correlations for all the variables in the two detrended studies. Ozone, NO_2, and temperature were also significantly correlated with total admissions. For respiratory admissions, all the variables except COH and relative humidity were correlated; for SO_2 and ozone, detrending resulted in an appreciable diminution of the apparent relationships. Removing the asthma admissions weakened most of these relationships, except for temperature. However, asthma admissions showed only weak correlations, at best, especially for children. Nonrespiratory admissions were highly significantly negatively correlated with temperature; the similar (but weaker) relationships seen for ozone and sulfate may be the result of their collinearity with temperature. Lag effects were more pronounced for respiratory admissions than for all diagnoses; either 24- or 48-hr lags usually produced slightly higher correlations.

Because of the similarity in the apparent relationships between several pollutants and respiratory admissions,

Bates and Sizto used multiple regression analysis to try to partition the effects. In the second and third papers (*70,71*), partial correlation coefficients were given rather than regression equations per se. The explained variance decreased markedly when annual detrending was introduced. A regression equation was given in a more recent paper (*73*). However, it featured separate terms for each of the various lags for temperature and air pollution, which can lead to some confusion in interpretation, especially when the signs conflict (using cumulative lags avoids this problem). Assuming that the mean values of lagged and unlagged variables are identical and summing the coefficients for various lag terms yields:

$$\% \text{ deviation in respiratory admissions} = -7.1 - 0.172\,T + 0.81\,SO_4^{2-} = -0.036\,O_3 \quad (R^2 = 0.056) \qquad (2)$$

Equation 2 is problematic because the three environmental terms are highly correlated with one another (positively) and each has a positive (bivariate) relationship with respiratory admissions, yet two of them show a net negative effect on admissions in the multiple regression. This is a symptom of collinearity, which can inflate both the regression coefficients and their significance levels (when collinear terms enter with opposite signs). Further, evaluating Equation 2 at the means of the independent variables yields −4.2% for the mean deviation, rather than the expected value of zero. According to this relationship, it appears that sulfate is the main contributor, and that its elasticity is somewhere between 4 and 8%. From contingency tables in an earlier version of the paper provided to me by D. V. Bates, I was able to estimate the elasticity of total respiratory admissions on sulfate as about 8%. This value is similar to those found in the other studies discussed above. Based on 40 respiratory admissions per summer day as an average, Equation 2 predicts that eliminating sulfate entirely as a causal factor would thus save two to three daily respiratory admissions for this population of about 6 million people. However, the validity of this prediction also depends on concurrent trends in the other collinear pollutants.

Data from Southern Ontario were also analyzed by Hammerstrom et al. (*11*), in an effort which emphasized statistical methodology. Time-series analysis were performed on a 6-year (1979–1985) database of daily hospital admissions, weather data, and concentrations of six different air pollutants. Twenty-four-hour averages were used for the gaseous species. The data were characterized by substantial serial correlation and nonnormal frequency distributions. Analyses were performed for respiratory admissions (causal hypothesis) and for admissions for gastrointestinal illness and accidents (control diagnoses). Statistical analyses progressed from simple bivariate correlations to bootstrapped correlation analysis to multiple regressions with autoregressive error modeling. In general, the numbers of significant correlations decreased as the level of complexity of the analysis increased. It was shown that bivariate correlations are inappropriate when seasonal trends are present in the data and that biased estimators can result when inappropriate models are used. For example, there were many more significant bivariate correlations between admissions for both respiratory and control diagnoses and air pollution than would be expected due to chance, but most of these disappeared when multiple regressions were used. Typically, only 1–5% of the variance in admissions was explained by the variables used in this analysis, even when weather effects were included in multiple regressions. The pollutants found to be significant in multiple regressions including various weather variables but only one pollutant species included ozone (summer and winter) and SO_2 and SO_4^{2-} (summer only). Total suspended particulate matter was not investigated in multiple regressions, but had the highest bivariate correlation with respiratory admissions. These results suggest that there are many other factors controlling the timing of hospital admissions; if any of them should be temporally correlated with air pollution, confounding and spurious correlation could easily result.

In a further account of this analysis, Lipfert and Hammerstrom (*74*) showed that 24-hr averages gave higher bivariate correlations than peak-hour averages, and that breaking up the large region into three subregions did not improve the precision of estimates. It appeared that the stability in admission rates achieved by pooling outweighed the loss in precision of air pollution exposure estimates. Based on multiple regressions using cumulative lags, it appeared that the elasticity of air pollution on July–August respiratory admissions was around 20%, which is considerably higher than estimates by Bates and Sizto based on individual lags.

The most recent work by Bates and colleagues deals with emergency room visits in Vancouver, British Columbia, from July 1984 through October 1986 (*75*). The study population was about 1 million people, served by nine hospitals for which the numbers of daily emergency room visits were pooled. Diagnostic categories were asthma, pneumonia, "all respiratory" (excluding common colds and upper respiratory infections), and all diagnoses. Data were recorded manually by the same individual for all nine hospitals to provide a consistent database. Air pollutants included maximum hourly values of SO_2, NO_2, ozone, COH, and 24-hr values for SO_4^{2-} aerosol. Daily maximum temperature was also included. The statistical analysis was limited to bivariate coefficients for lags of 0, 1, and 2 days, by age group and diagnosis. In summer, temperature and ozone were significantly correlated with total visits (all diagnoses) for all age groups; the authors felt that the ozone correlations (which were always weaker) simply reflected the expected relationship between ozone and temperature. Sulfur dioxide and SO_4^{2-} were correlated with asthma and total respiratory visits, mainly for ages 15–60. In winter, results were similar with somewhat weaker associations; temperature was also positively associated with emergency room visits for all diagnoses, up to age 61. However, since seasonal trends were not completely removed from this analysis, the results must be viewed with caution. Within each 6-month period, seasonal trends (due to nonpollution factors) could create artifacts in either direction. For example, the normal winter cycle in

respiratory disease coincides with cold weather, space heating emissions, and reduced atmospheric mixing. Thus, an air pollutant associated with space heating would be collinear with this within "season" trend. In summer, the opposite effect may obtain, in that the normal summer ozone and sulfate peaks would coincide with a dip in respiratory disease. Thus the true daily pollution effects may actually be stronger in summer than indicated by this analysis.

A "spike" in asthma emergency room visits was seen in all three Septembers in Vancouver, confirming other observations about the importance of the fall season. For example, respiratory admissions were very high in October in the study of Levy et al. (*68*) in Hamilton, Ontario. The Vancouver spikes were not associated with any of the air pollutants measured in this study; in 1 year, the rise in asthma visits followed a sharp drop in temperature, which conforms to the hypothesis of Goldstein and Block (*76*) (discussed below).

Maarouf and Zwiers (*77*) analyzed 5 years of daily emergency admissions to 26 hospitals in metropolitan Toronto for asthma, bronchitis, and emphysema, in relation to relative humidity and the nitrate fraction of TSP. The reasons for selecting these independent variables were not given. They chose the mid-September to mid-December period for analysis because of generally higher and more variable admission rates during this period (about 18 per day). Their analysis accounted for day-of-week and long-term trends as well as for occasional outliers with high admissions followed by low admissions on the next day. One of their techniques used a case–control method, where cases were defined as the highest 10% of admission days and controls as the lowest 10%. The environmental conditions were then compared as a function of lag for both groups. The authors concluded that respiratory admissions were associated with both relative humidity and suspended nitrates, but they performed no multiple regressions.

Studies by Knight et al. in Prince George, British Columbia, offer the opportunity for direct comparisons of admissions (*78*) with emergency room visits (*79*), for a single regional hospital. A 2-year period from 1984 to 1986 was studied, emphasizing respiratory diagnoses in three broad categories: asthma, lower respiratory diseases (LRD = bronchitis, emphysema, chronic obstructive lung disease, etc.), and other (influenza, pneumonia, upper respiratory diseases, etc.). The study was limited by the sparse air-quality data available, consisting of SO_2 (which was not used because of a change in methods part way through the period), total reduced sulfur (TRS), and TSP measured every sixth day (with no coverage on the other five days). Total reduced sulfur, which includes H_2S, was of interest in this community because of the presence of local pulp mill sources. The statistical analysis accounted for day-of-week and seasonal trends and used a log-linear Poisson model. The absolute numbers of admissions or emergency room visits were low, with counts of zero on many days. Respiratory admissions were dominated by children. The ratio of emergency room visits to admissions was about 2 for asthma, 3–4 for LRD, and about 6 for others. There were no associations between admissions and emergency room visits other than common temporal patterns, suggesting that the underlying populations and causal factors may be different. The associations with air quality were described as "quite small." For admissions to hospital, TRS had no association, and the TSP association failed to reach significance (with lags of up to 3 days). For respiratory emergency room visits, TRS was significant with a lag of 2 days ($t = 3$), and TSP was significant for asthma and "other" visits, also with a lag of 2 days. Since log-linear models were used, elasticities depend on the magnitude of the pollution variable; a 10% reduction in TRS was associated with an elasticity of 5%; a 75% reduction, with an elasticity of 9%. The elasticities for TSP were about twice as high but less certain. Analysis by season showed the associations to exist only in winter, which is the time of highest air pollution. This is in contrast to the Ontario studies, which found significant results only in summer.

Studies of Asthma in Various Cities. Asthma hospitalizations were included in several of the studies reviewed above, but generally were among the weaker relationships with air pollution. The recent increases in asthma mortality and morbidity (*80*) make this topic particularly relevant; a number of studies emphasizing the timing of asthma hospitalization are reviewed below.

Goldstein and co-workers (*76,81–84*) have investigated temporal and spatial relationships of asthma in New York City as measured by emergency room visits. The first paper (*76*) used conventional multiple regression methods for relatively small samples ($n = 40$–104) from the fall seasons of 1970 and 1971, testing the hypothesis that the number of emergency room visits for asthma was associated with temperature and daily average SO_2. The hypothesis was accepted for Brooklyn but not for Manhattan. Because no account was taken of lags, or day-of-week or seasonal effects, this finding appears problematic. In subsequent papers (*81–84*), Goldstein et al. developed statistical methods based on the frequency distributions of visits, without *a priori* consideration of the pollutant distributions. Goldstein and Dulberg (*82*) and Goldstein and Weinstein (*84*) investigated a period of greatly decreasing SO_2 levels (1969–1972) using selected data from the 40-station New York City monitoring network; they were unable to find a relationship between emergency room visits for asthma and either 24-hr averages of SO_2 and COH or hourly SO_2 peaks. (Hourly SO_2 concentrations as high as 0.5 ppm were experienced during this period.) This finding is consistent with Greenburg et al.'s observation that there was no increase in emergency room visits for asthma during the November 1953 air pollution episode (*85*). Goldstein and Weinstein (*84*) also concluded that days with peak hourly values did not necessarily coincide with days of high 24-hr average SO_2. No other pollutants were investigated, in spite of a previous finding (*80*) that peak days for asthma tended to coincide throughout the city, suggesting either a weather variable or a regionally distributed pollutant such as SO_4^{2-} or ozone. Given the regular occurrence of asthma episodes in the fall in different cities, weather factors are likely to be important.

Girsh et al. (*86*) studied children's emergency room visits for asthma in Philadelphia from July 1963 to May 1965. Visits were found to increase by a factor of 9 on stagnant days with high barometric pressure and high air pollution. Although no data were given in the paper, mention is made of measurements of NO_x, SO_2, CO, total oxidants, dust, and pollen counts (during the ragweed season). The hospital studied was located in an area of high dust loading. Asthma attacks were not found to be associated with pollen counts or with the peak incidence of upper respiratory infections. The authors reported that no specific pollutant could be "incriminated" and that total oxidants seemed to be least important.

New Orleans' reputation for asthma epidemics prompted attempts to try to identify any associated environmental agents. During some episodes, emergency room admissions increased by an order of magnitude, and asthma deaths were reported. The study reported by Lewis et al. (*87*) ran from June 1960 to June 1962, and included a census of an area thought to have a number of susceptible persons, time-series analysis of hospital emergency room treatments, and local monitoring of airborne particles. The results reported included a lack of correlation between air pollution and asthma attacks among 67 selected patients in the census area or between attacks in this group and emergency room treatments for the population at large. A statistically significant relationship was reported between emergency room visits and particles identified as due to "poor combustion, with silica." These particles were reported to be in the size range > 4 μm; uncontrolled refuse dump fires were the suspected source.

The results of Khan (*88*) in Chicago were generally consistent with the findings in other cities. The relationship between daily attacks and emergency room visits or hospitalization was weak ($R < 0.4$) even for the same subjects. The proportion of asthma variance associated with air pollution was small (5–15%). However, the most significant air pollutant with respect to asthma attack frequency was CO, which seems counterintuitive.

A panel study of 34 asthmatics in Los Angeles from August 1977 to May 1978 (*89*) found only 10% "responders" (subjects with a statistically significant relationship between symptoms or need for medication with air pollution). Sulfate was the most significant pollutant for these three subjects. Thus it appears that only a fraction of even a sensitive subpopulation is likely to respond to daily variations in air pollution. This helps explain the small magnitudes of the effects reported in these various morbidity studies and the need for long time periods or large populations. A later, more comprehensive analysis of Los Angeles asthmatics by Whittemore and Korn (*90*) found both oxidants and TSP to be significant predictors of asthma attacks, based on 24-hr averages and a multiple logistic regression model. The magnitude of the effect was small, on average: a 25% excess risk of an attack was associated with either about 0.12 ppm increase in oxidants or 250 $\mu g/m^3$ in particulates. (Note that this dose–response function, 10% per 100 $\mu g/m^3$, is consistent with the episode slope of Figure 1, given the higher frequencies of attacks with respect to hospitalization.) The authors pointed out that, because of collinearity, TSP was intended to be a surrogate for all particulates, SO_x, and NO_x. The most important predictor was an asthma attack on the preceding day, which underscores the importance of dealing with serial correlation in this type of study. Also, the most likely day for an attack to be reported was the last day of the weekly reporting period, which raises the possibility of subjective bias. Such a reporting artifact could mask any true relationships but would be less likely in studies of hospitalization.

Richards et al. (*3*) studied childhood asthma from August 1979 to February 1980 in Los Angeles, using data on emergency room visits, hospital admissions, and subjective symptoms. Monthly visits and admissions were highest in winter, in spite of a smog episode in September and the findings of other studies (discussed above) of peak asthma attacks in the fall. However, because of the differences in climate, this finding provides support for the hypothesis of Goldstein and Block (*76*) that asthma attacks increase with the advent of the first cooler days of the season. On a daily basis, emergency room visits were positively correlated with COH, NO_x, hydrocarbons, TSP (not significant), days with Santa Ana winds, and allergen counts. Significant negative associations were found with ozone, SO_2, temperature, relative humidity, and sulfate (not significant). These relationships were combined by means of factor analysis; three factors explained 30% of the variance in numbers of asthma emergency room visits. These ambiguous findings may be due in part to the failure to control for day-of-week or seasonal trends or to consider the simultaneous variations of temperature and air pollution.

White et al. (*91*) conducted a pilot study of the effect of ozone on children's visits to the emergency room of a large inner-city public hospital in Atlanta for asthma or reactive airway disease, from June through August 1990. Ozone data were available from two monitoring stations. This study did not develop a consistent dose–response relationship between respiratory emergency room visits and ozone, but did report 38% more visits on 6 days for which peak ozone exceeded 0.11 ppm ($p = 0.04$). The study may have been compromised by lack of controls for day-of-week and seasonal effects, in addition to the short time span covered.

Frequencies of asthma attacks were studied by Pönkä (*92*) using admissions to Helsinki hospitals from 1987 to 1989. Emergency admissions for asthma were studied separately. The cases analyzed were limited to ICD-9 493 (bronchial asthma); chronic bronchitis was excluded. The air pollution variables and the numbers of monitoring sites included SO_2 (4 sites), NO and NO_2 (2 sites), CO (2 sites), ozone (1 site), and TSP (6 sites). Levels were generally low (the average SO_2 was 19.2 $\mu g/m^3$, but the average TSP was 76 $\mu g/m^3$) and 24-hr averages were used in the analysis. Data were also collected for temperature, humidity, and wind speed at one station. Logarithmic transforms were used in addition to linear models. Seasonality was accounted for by standardizing for minimum daily temperature and by multiple regression. The most significant

pollution variables, after temperature correction, were NO, NO_2, ozone, and CO; SO_2 and TSP were not significant. Elasticities were not given, but I estimated typical values to be around 12% on a same-day basis. Log-transformed variables were reported to fit slightly better. For ozone, the results for 1- or 2-day lags were much stronger than for the same day; lags greater than 2 days were not studied. Results were also presented for three different age groups; 21 of the 36 pollution correlations were significant ($p < 0.05$); the strongest affects were seen in adults (ages 15–64 and 64+). Pönkä concluded that traffic-related pollution seemed to be the most important in Helsinki, but no explanation was offered for the lack of response to the fairly high levels of TSP.

Cody et al. (*93*) analyzed asthma and bronchitis visits (all ages) to emergency rooms of nine northern and central New Jersey hospitals for the summers (May–August) of 1988 and 1989. The method of analysis followed that of Bates and Sizto (*8*) in that data from all the hospitals and from five ozone monitoring stations were pooled to create a single regional time-series for each year. However, unlike the Bates and Sizto study, it appears that all the hospitals in the region were not included. Emergency room visits for finger wounds were used as a control variable. Other environmental variables in the analysis included SO_2 (24-hr average), PM_{10} (every sixth day), daily mean temperature and relative humidity, and atmospheric visibility measured at Newark at noon. Ozone was averaged from 10 AM to 3 PM each day. Day-of-week effects were examined by replicating the analysis with weekends excluded. A similar approach was used to remove precipitation effects on visibility, by deleting precipitation days. Regression analyses were performed separately for each year and for the pooled data set ($n = 226$). Lags up to 2 days were considered. Ozone was significantly higher in 1988, but the average daily emergency room visits for asthma and bronchitis were lower. Because there were fewer than 5 daily emergency room visits for asthma or bronchitis on average, a Poisson regression model would have been preferable.

The statistical analysis consisted of bivariate correlations and various multiple regression models. There were no statistically significant relationships for bronchitis visits or for finger wounds. For asthma visits, the only significant relationship was the negative effect of temperature (probably representing seasonal effects); the method chosen to account for this was stepwise multiple regression. Since the correlation between ozone and temperature was much stronger ($R = 0.64$) than either between asthma visits and temperature ($R = -0.23$) or ozone (R values from 0.08 to -0.12, depending on lag), the method of accounting for seasonality in the data could be important.

However, after accounting for the temperature effects, Cody et al.'s multiple regression results showed a significant relationship between ozone and emergency room visits for asthma that was stronger in 1989 than in 1988, in spite of the lower average ozone concentrations in 1989. While there was no significant difference in the temperature regression coefficients between the 2 years, 1989 showed both same-day and 1-day lagged ozone to be significant, with a combined elasticity of 73 ± 28% (two-σ limits), while 1988 showed only 1-day lagged ozone to be significant, with an elasticity of 41 ± 28%. The elasticity of asthma emergency room visits on 1-day lagged ozone for the combined data set was 27 ± 19% (2-σ limits). For comparison with studies reviewed above, this regression coefficient corresponds to about 28% excess visits per 100 $\mu g/m^3$. Accounting for serial correlation had only minor effects on the analysis, as did omitting weekends. No other environmental variables were significant in multiple regressions.

I used the coefficients for temperature and ozone from the pooled data set to estimate the long-term difference between the two summers. This analysis predicted a decrease of 0.14 visits per day based on environmental factors; there were actually 0.5 more visits per day in 1989, which suggests that there are other important factors controlling the frequency of asthma emergency room visits. It is also possible that the results of Cody et al. are sensitive to the method of seasonal adjustment, since it is expected that the indicated effect of temperature on asthma emergency room visits is at least in part a surrogate for other environmental influences such as the presence of pollen, rather than temperature per se.

In summary, few of the studies of the timing of hospitalization for asthma provide convincing evidence of relationships with air pollution, in part because of shortcomings in study designs.

Other Time-Series Studies. Kevany et al. (*94*) analyzed mortality and hospital admissions in Dublin for the winters of 1970–1973, examining partial correlations for respiratory and cardiovascular causes in relation to smoke and SO_2, mainly for the winter of 1972–1973. Respiratory admissions showed more significant correlations with smoke than with SO_2. Influenza admissions were not associated with either pollutant. Cardiovascular admissions were highly significant for both smoke and SO_2 for males; results for females were mixed. Kevany et al. corrected for temperature effects, but the report was unclear as to how day-of-week effects were handled. Lags varied from 0–3 days. Collinearity between smoke and SO_2 was not reported, but the authors noted declining long-term trends for smoke and increasing trends for SO_2, which may have helped to separate the pollutants.

Ozkaynak et al. (*95*) presented a brief account of a study of hospital admissions in Boston and three other Massachusetts cities as part of the development of a health-based air quality/visibility index for the state. Data were pooled for four cities (Boston, Worcester, Springfield, and Fall River/New Bedford) following the methodology of Bates and Sizto (*8*). The authors report that many models were developed and that both positive and negative relationships were seen for the various respiratory diagnoses. Examples were shown linking pneumonia/influenza admissions with 24-hr lagged ozone for adults in summer and with 24-hr lagged TSP for children in winter ($p < 0.01$). The earlier report on this project (*96*) illustrates some of the pitfalls and general observations seen in many of the other studies reviewed above: *a*) no single pollutant is identified as most important for respiratory admissions, *b*)

daily averages are usually more significant than daily peaks, *c*) results are unreliable for the smaller populations (including children's admissions), *d*) seasonal and temperature effects are important, especially for upper respiratory and pneumonia/influenza admissions, and *e*) collinearity can result in regression coefficients for related pollutants with opposite signs, in the same regression.

Autocorrelation was not considered, nor were results given for control diagnoses, although, because no pollutants were significant for cerebrovascular admissions, this category may have in fact served as a control for respiratory admissions. The pollutant elasticities for respiratory admissions were higher (0.10–0.30) than in most of the studies reviewed above, even though day-of-week and seasonal effects were accounted for with dummy variables. Multiple regression R^2 values were in the range of 0.1–0.6 (including day-of-week and seasonal effects); pollutant partial R^2 values were in the range 0.02–0.04.

Daily emergency room visits in Barcelona were studied by Sunyer et al. (*97*) for 1985 and 1986. Diagnoses were limited to chronic obstructive pulmonary disease (COPD), and data were collected from four large hospitals which accounted for about 90% of all emergency room visits in Barcelona. The emergency room data were screened by a clinician to ensure proper diagnosis classification based on a list of symptoms and averaged about 12 visits per day. Air pollution data were obtained from a citywide network for SO_2 and British smoke (24-hr averages from 17 stations); data on SO_2, CO, NO_2, and ozone (1-hr maximum values) were obtained from the average of two stations. Meteorological data were collected from five different monitoring stations. Pollution levels were within the European Community Guidelines, but World Health Organization guideline values were exceeded on occasion.

The paper presents bivariate correlations between emergency room visits and air pollution, but these results were influenced by seasonal confounding. When stratified by temperature, the relationships between emergency room visits for COPD and 24-hr SO_2 and smoke were about the same and were stronger in warm weather. The potentially confounding effects of meteorology season, and day-of-week were handled by adjusting the emergency room-visits variable. After adjustment, SO_2 (either 1-hr or 24-hr measures) was significantly associated ($p < 0.01$) with daily emergency room visits for COPD on the same day and lagged 1 day. The relationship was weaker and lost significance for a 2-day lag; cumulative lag effects were not reported. The smoke and CO variables were also significant ($p < 0.01$), but the NO_2 and ozone were not. Accounting for serial correlation made little difference in these results.

The elasticity for SO_2 on a single-day basis was about 9.5%; estimated values for smoke and CO were 6 and 5%, respectively. Rough estimates of the 2-day values would be about double these figures. In an effort to identify a threshold of no effect, Sunyer et al. successively truncated the data set to remove SO_2 values above certain cut-off points and then reevaluated the regression slope (after adjustment for potential confounders as above). The results of this exercise are shown in Figure 16 in terms of elasticities (based on 11.9 COPD visits per day in all cases).

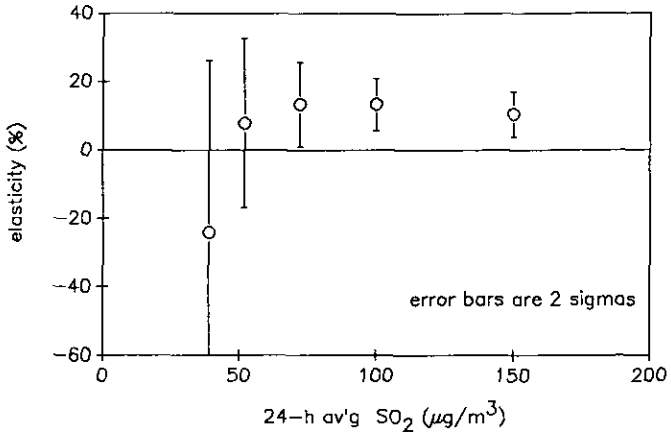


FIGURE 16. Elasticity of emergency room visits for chronic obstructive pulmonary disease in Barcelona as a function of SO_2 level. Data points are not independent but were created by successively truncating the data set. Data from Sunyer et al. (*97*).

The slopes were statistically significant for daily SO_2 values in excess of about 70 $\mu g/m^3$, which is well below most air quality standards.

In an invited commentary on Sunyer et al.'s report (*97*), Corn (*98*) tried to place these findings in a risk-analysis context and expressed doubt that air-quality standards could actually "ensure zero risk to all members of the exposed population." In their rebuttal, Sunyer and Anto (*99*) pointed out that errors in estimating the actual pollution exposure likely biased the true relationship downward and that subsequent extension of the data set for three additional years produced similar findings, in spite of lower pollution levels.

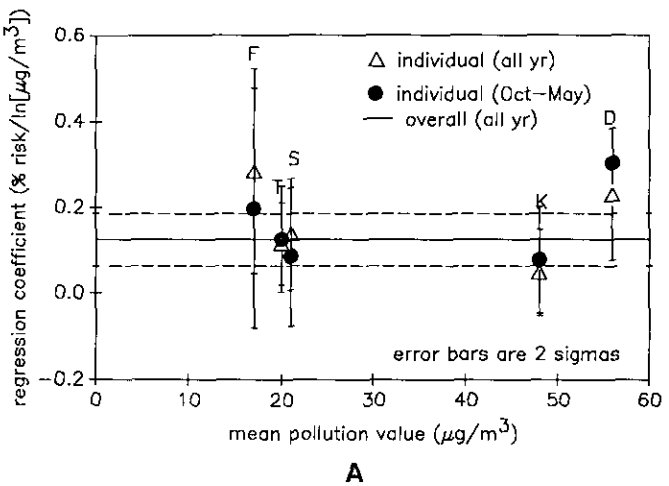
Schwartz et al. (*100*) considered cases of children's croup and bronchitis documented by hospitals and physicians over a 2-year period in Duisburg, Köln, Stuttgart, Tübingen, and Freudenstadt, Germany. Not all of these cases resulted in admission to the hospital. Pollutants considered were 24-hr averages of SO_2, NO_2, and TSP (measured by a β-gauge tape sampler). Data from one to four monitors were averaged for each city. Weather variables included mean temperature and relative humidity. Each city was studied separately, and then all five were pooled, taking into account the variance within and between cities. The method of statistical analysis employed Poisson regression (because of the relatively low daily case counts) and a two-stage analysis approach. The case counts were first fit to weather, seasonal, and other temporal variables; air pollution variables were then fit to the residuals for each city and serial correlation was accounted for using autoregressive methods. To account for the loss of data due to physicians dropping out of the study, variables for time or for the numbers of reporting physicians were included in each model. After seasonal effects were accounted for, weather variables were not significant.

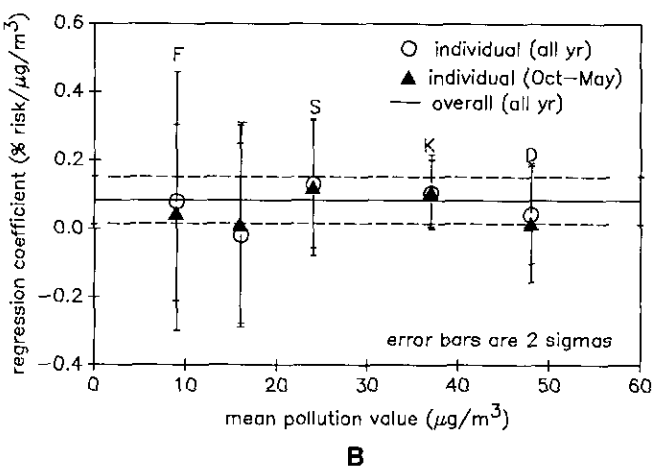
No significant pollution associations were reported for bronchitis. The results for croup showed that all three

pollutants were statistically significant ($p < 0.05$) when the five cities were pooled (the logarithm of TSP was found to fit better than the linear measure). Log TSP was significant in four out of five individual cities, NO_2 was significant in two, while SO_2 was only significant in Köln (where neither TSP nor NO_2 was significant). The analysis was repeated for the months from October to March (the high pollution months), and the results were quite similar. Serial correlation effects were reported to be small. The average of same-day and 1-day lagged pollution was reported to have the same predictive capability as same-day alone, but it was not reported whether the magnitude of the response increased when lags were included (as would be expected).

The pooled elasticities (at the mean) for log TSP, NO_2, and SO_2 were 9.4, 16.9, and 2.2%, respectively; use of the log transform for TSP reduced the elasticity somewhat. Figure 17 plots the regression coefficients against mean pollution values for each city to display dose–response relationships. The plots for SO_2 and NO_2 suggest the possibility of thresholds around 30–40 $\mu g/m^3$ (which was also seen in the plot of pollution quintiles for NO_2 presented by Schwartz et al.). Note that a trend of regression coefficient increasing with decreasing pollution levels suggests a surrogate model. The plot for TSP more closely resembles a linear, no-threshold model, since the regression coefficient tends to remain constant over the whole range of mean values. The effects of NO_2 appeared to be stronger than the other pollutants, which would be further emphasized if a threshold were considered. Schwartz et al. (*100*) noted that NO_2 had been linked with decreased resistance to respiratory infection in clinical experiments at much higher concentration levels. They also noted the weak effects of SO_2 and suggested that they may have been the result of collinearity with the other pollutants.

Miscellaneous Studies. Nobel et al. (*101*) analyzed police ambulance runs and emergency unit visits to three Boston nonprofit hospitals in 1968 in relation to weather variables, days of the week, holidays, and holiday travel





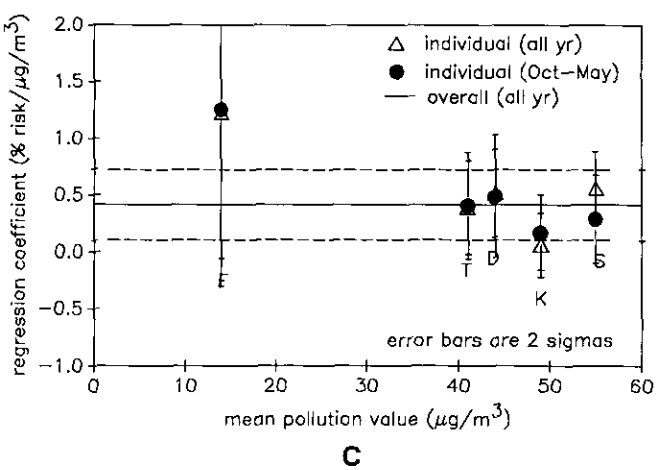


FIGURE 17. Regression coefficients for children's croup and bronchitis in five German cities (D, Duisburg; K, Köln; S, Stuttgart; T, Tübingen; F, Freudenstadt). The horizontal solid line represents the coefficient for all five cities pooled; the symbols refer to the regression lines for each city. (*A*) log total suspended particulates, (*B*) SO_2, (*C*) NO_2. Data from Schwartz (*100*).

patterns. The dependent variables all included trauma events, although one category of visits was defined by subtracting the traffic accidents. The only independent variable that might be related to air pollution was "occurrences of smoke or haze," which was not significantly correlated with any of the dependent variables. The patterns that emerged from this analysis were day-of-week and holiday effects, a tendency for more emergency room visits during warm, sunny weather, and possible adverse weather effects on traffic accidents. Adverse weather, such as precipitation or fog, did not have a negative impact on emergency room visits, as had been hypothesized by Carnow (*53*).

Nagata et al. (*102*) analyzed daily data on acute respiratory and digestive diseases using insurance records from July to September 1975 for two Japanese industrial cities on the island of Honshu. To preclude day-of-week effects, only data for Tuesdays through Fridays were used. Lags up to 10 days were studied, for maximum SO_2 and oxidant concentrations and several weather variables. The two locations had similar climates and maximum oxidant levels (means of 0.065 and 0.079 ppm), but different maximum SO_2 levels (means of 0.022 and 0.008 ppm). Only bivariate correlations were made, and no seasonal corrections were used (from the scatterplots, seasonal effects appeared to be modest).

For respiratory disease, the high-SO_2 area showed significant correlations with maximum SO_2 for lags of 4, 6, 7, 8, and 10 days, and with maximum temperature for a lag of 6 days. The low-SO_2 area had significant respiratory correlations only for maximum temperature for lags of 5 and 7 days. For acute digestive diseases (presumably intended to be controls), both areas showed a significant correlation with maximum SO_2 (lags of 3 and 5 days, respectively, at the 0.01 level for the low-SO_2 city). There were also scattered significant correlations for digestive disease and weather variables, three at the 0.05 level and one at the 0.01 level. This study may be an example where more restrictive probability levels should be used to allow for the problem of multiple interferences and the large number of correlations presented (*103*). If the lags are considered to be independent, which depends on the degree of autocorrelation, 264 correlations are presented and one would expect to see 2–3 significant at the 0.01 level and about 13 at the 0.05 level. In fact, there were three values at the 0.01 level and 12 more at the 0.05 level, so on this basis, the results could be entirely due to chance. The only compelling arguments to the contrary are the findings of 40 positive correlations for respiratory disease versus temperature and SO_2 and only four negative values. There were no significant correlations for oxidants and either disease (25 positive and 19 negative values). If the association of respiratory disease with SO_2 is taken at face value, then an argument can also be made for including lags longer than 1–3 days, although the period of time between exposure and taking action on symptoms could also have been a cultural component.

Strahilevitz et al. (*104*) examined the associations between daily use of a psychiatric hospital and air pollution in St. Louis during the summer and fall of 1979. Pollutants included COH, oxidants, hydrocarbons, CO, NO_x, and SO_2. No weather variables or seasonal corrections were included, but a significance level of 0.005 was selected to allow for the problem of multiple inference. Three groups of days were examined: all days, weekends and holidays, and all other days. CO was positively associated with emergency room visits by all patients for all days ($p < 0.005$); NO_2 was positively associated ($p < 0.01$) with admissions for alcoholics on all days. Since both of these species are associated with vehicle emissions, which are usually lower on weekends as are psychiatric admissions, and significance was only found on all days, it is possible that these findings were influenced by the weekday/weekend patterns.

Giles (*105*) reports an attempt to find meteorological correlates of asthma in Tasmania, including hospital morbidity. Meteorological factors included wind chill and discomfort and the analytical technique was that of seeking coherence among the time series. No such relationships were found.

Hospital records from November to February 1979 in Bombay were examined by Bladen (*106*) for the city as a whole and for various subareas. The analysis was limited to "acute respiratory disease related to bronchitis, emphysema, and asthma." Air pollution species included SO_2, particulates, CO, and hydrocarbons. No seasonal or temperature adjustments were described, nor were results given for individual pollutant species. The bivariate correlations were in the range of 0.50–0.75 (monthly averages) and peaks in both air pollution and admissions were reported to occur at times of thermal inversion. No data were reported on concentration levels.

Meteorological variables were also emphasized by Diaz-Caneja et al. (*107*) in their study of air pollution effects on hospitalization in Santander, Spain. They considered admissions to a single hospital for heart failure and COPD from 1979 to 1982 in response to daily smoke and SO_2 averaged over three monitoring stations. Meteorological variables included barometric pressure, temperature, relative humidity, rainfall, number of calm hours, and wind speed and direction. Since the average number of daily admissions was of the order of one or fewer, a Poisson model should have been used in this study. The stepwise regression models considered these variables raised to various exponents, from 0.25 to 2, lags up to 2 days, and seasonal variations. Same-day effects were found to be the most important. The regression results were difficult to interpret because significance levels were not given and some of them employed the same variable with different exponents, which entered with opposite signs. However, the authors plotted average admissions for groups of days according to their average pollution levels, which provided a basis for estimating linear dose–response functions. Such estimates will be overestimates because they do not take into account covariables or seasonal cycles. On this basis, heart failure admissions were not significant, COPD admissions were marginally significant, and their total was significantly associated with smoke. The elasticities estimated on this crude basis ranged from 14 to 47%, which seem high, but elasticities based on the author's

regression results were even higher. In summary, it appears that there may be a relationship between smoke pollution and hospitalization in Santander, but the details of this relationship cannot be deduced from the results presented.

Maarouf (*108*) used an episodic analysis approach to examine children's respiratory hospital admissions in Toronto during a 10-day period in October 1982, which included peak values of several air pollutants. He found that admissions peaked 2 days before the highest air pollution values and concluded that the population of susceptible patients may have been depleted by the first part of the episode. However, the 10-day mean admissions during this period were no different from the monthly mean, so that it is entirely possible that only random fluctuations in admissions were seen during this event (the peak daily admissions were reported to be about two standard deviations above the mean). Maarouf's analysis illustrates the possible pitfalls that may be encountered when looking for weak effects in a small data set.

Cross-Sectional Studies of Hospitalization

The time-series studies reviewed above pertain only to the timing of hospital admissions, not to the underlying rates of disease prevalence. The traditional method of analyzing chronic responses is by means of geographic (cross-sectional) analysis. Studies of this type are reviewed in this section. One must also realize that chronic or long-term studies should reflect the long-term sums of short-term effects. Failure to achieve this consistency could indicate that positive short-term effects (due to air pollution, for example) were canceled by subsequent negative responses.

Pittsburgh Area. Carpenter et al. (*109*) performed a cross-sectional analysis of hospitalization costs in Allegheny County, Pennsylvania (Pittsburgh) for 1972. The observations were drawn from about 38,000 admissions to 28 hospitals, for respiratory causes (ICD 462–515.9, which includes some upper respiratory causes and tonsil/adenoid problems), "suspect" circulatory diseases (ischemic heart diseases, acute cerebrovascular diseases, etc.) and "comparison" (i.e., controls) circulatory diseases (rheumatic fever, hypertension, etc.). The average hospitalization rate for respiratory diseases was 5.8/1000, ranging from 3.9 to 10.6/1000 among the various subgroups defined by air pollution levels. This compares with a value of about 4.0 from Pope's study in Utah (*65*), although there are some slight differences in the ICD codes included. Air pollution exposures and socioeconomic variables were obtained from the corresponding census-tract data (air quality measurements from 49 SO_2 monitors (sulfation plates), and 21 TSP stations were interpolated to census-tract centroids. Data on smoking habits were not available. Sixteen demographic groups were identified by race, sex, and age grouping, and the regression analysis used membership in these groups as independent variables explaining hospitalization rates for the entire population (admissions/1000). Young children were not singled out for special consideration, which is unfortunate given their high rates of respiratory illness and their lack of smoking. The associations between respiratory disease admission rates and SO_2 and TSP were just significant at the 0.05 level. The effects of TSP and SO_2 were about 0.27 and 0.71 annual admissions/1000 population, or about 6 and 12% per 100 $\mu g/m^3$, respectively. These figures are similar to the results obtained with the time-series analyses discussed above, which suggests that any confounding variables remaining in this data set (such as smoking habits, for example) had only modest effects. The corresponding elasticities are 5 and 12%, which should be added for comparison to studies that assigned the entire effect to a single pollutant. Neither of the circulatory disease categories was significant, although the suspect categories were close for TSP ($p = 0.07$).

A corresponding analysis of lengths of hospital stay also found significance for respiratory diseases and air pollution exposure ($p = 0.03$) and for certain circulatory diseases ($p = 0.009$). This portion of the study was able to account for smoking habits because it dealt with the population of patients, not with the county population as a whole. Smoking was significant at the $p = 0.001$ level for respiratory diseases. The pollutant effects on lengths of stay were not consistent with dose–response relationships and were of the order of 1 extra day for an additional 20 $\mu g/m^3$ of particulates.

Maine Mill Towns. A cross-sectional study of occupational and community exposures to pulp and paper mill effluents (as measured by residential proximity to the source) was conducted by Deprez et al. (*110*) for Maine mill towns. Hospitalization diagnoses included respiratory infections and inflammations, respiratory cancer, chronic obstructive pulmonary disease, bronchitis and asthma, respiratory signs and symptoms, all respiratory combined, myocardial infarction (controls), and total admissions. Age- and sex-adjusted rates were computed for use in bivariate correlation computations. All but the first two diagnostic groups were significantly correlated with occupational exposure, as indicated by the proportion of a town's work force employed in the production process. No category was significantly correlated with distance to the mill, which was interpreted as lack of a community exposure relationship. The authors stated that potential confounding by smoking and health insurance factors should be examined.

New York City versus Los Angeles. Noting that Northeastern patients tend to stay longer in hospital than West Coast residents, Knickman (*4*) studied population samples from New York and Los Angeles obtained from the 1974–1976 Health Interview Surveys (*111*). He noted that the admissions rate was higher in Los Angeles, but the average lengths of stay and the numbers of patient-days were higher in New York. A subgroup of patients with hospital stays longer than 50 days was defined for this study. Knickman studied the components of the geographic difference, including population variables (age, race, sex, income, education, marital status, diagnoses, and the long-stay patient subgroup. He found that this subgroup was responsible for most of the difference between the two samples. After excluding the long-stay patients, he stan-

dardized for these variables, which reduced the difference in patient-days between the two locations from 13.3 to 3.9%. This remaining difference was attributed to difference in medical practices. This study illustrates the importance of accounting for the population characteristics when comparing across areas. It is possible that a portion of the apparent air pollution effects found in the Pittsburgh cross-sectional study (*109*) may be due to artifacts arising from demographic differences in the subpopulations.

Combined Cross-Sectional and Time-Series Study in Ontario. Plagionnakis and Parker (*112*) pooled annual data from nine Ontario Counties from 1976 to 1982 in a combined cross-sectional time-series study of mortality and morbidity. These counties included the southern metropolitan areas and the locations around major point sources of SO_2 (Algoma and Sudbury); the latter were not included in the time-series studies of Southern Ontario described previously. Both total rates and respiratory (all subdivisions from ICD 460–519) diagnoses were analyzed. Two morbidity measures were used: annual admissions per 100,000 people and annual hospitals days per person. A linear trend variable was included for time; dummy variables were investigated for each county but were found to be nonsignificant and thus were dropped from the model. Logarithmic transforms were used for all variables. The pollutants investigated were annual average and 24-hr maximum values of TSP, SO_2, and SO_4^{2-}. The socioeconomic variables investigated included age (percent 65 and over), education, income, smoking, alcohol consumption, medical staff per capita, and the population of each county (to serve as an index of urbanization).

For annual hospital days, the models included population, time, percent > 65 years old, alcohol consumption, and various pollutants. The pollution regression coefficients were sensitive to the inclusion of these variables. For total hospital days, the best models used 24-hr maximum SO_2 (maximum value about 800 $\mu g/m^3$) and had an elasticity of about 8%. For respiratory hospital days, R^2 values were lower but elasticities were higher (up to 30% for SO_2). For total admissions, the model included numbers of medical staff per capita, which had a negative coefficient. Maximum 24-hr SO_2 again provided the best regression results, with an elasticity of 12–17% for total admissions and 15–26% for respiratory admissions. Neither TSP variable was significant (maximum 24-hr average about 300 $\mu g/m^3$), and annual average SO_4^{2-} was never significant for annual hospital days. Maximum 24-hr average SO_4^{2-} (maximum = 90 $\mu g/m^3$) gave slightly better results than annual average SO_4^{2-}, but the overall R^2 values were about the same as with SO_2. The finding of better results for maximum 24-hr readings than for annual averages could be interpreted as suggesting that this model might be measuring the annual sum of acute events.

British Children. Douglas and Waller (*113*) conducted a survey of the respiratory health of British children up to the age of 5 years. The survey included questions on symptoms and hospitalization; the data were based on 3131 families with consistent residential air-pollution exposure histories. The survey data on hospital admissions were

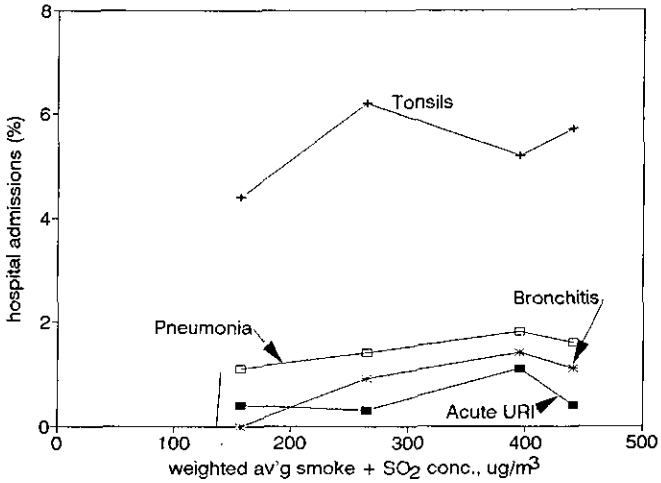


FIGURE 18. Percentage of British families with children admitted to hospital for various respiratory diagnoses as a function of estimated average pollution exposure. Data from Douglas and Waller (*113*).

corroborated with the hospitals concerned. Air pollution exposures were estimated by means of classification into one of four categories based on coal consumption. The available SO_2 and smoke monitoring data were then averaged to provide exposure estimates for each category. Differences in social class between the four groups were minimal. I cross-plotted these data in Figure 18 to check for consistent dose/response relationships. The rates of hospitalization (cases per 100 children) were lower than comparable U.S. rates and much lower than Canadian rates (*114*), in spite of the fact that all of the average pollution levels were above the current U.S. primary standards.

The authors concluded that a relationship had been shown between air pollution and lower respiratory tract infections, but not for the upper tract (acute UR infections and tonsillitis). In order to evaluate the data set statistically, I pooled all four diagnoses and regressed against both SO_2 and smoke levels (dummy variables for the different diagnoses were included). Both pollutants were significant (one at a time), and it was not possible to select the better measure. The elasticities were about 40% (i.e., 40% of children's respiratory hospital admissions were attributable to air pollution). However, the slopes were lower than Carpenter et al. obtained in Pittsburgh (*109*), perhaps because of the errors induced by estimating air pollution exposure. It is unfortunate that Douglas and Waller did not evaluate these data on the basis of individual responses and air pollution exposures, which would have had much greater statistical power.

German Children. Mühling et al. (*115*) classified children up to age 4 who visited a pediatric clinic from 1979 to 1982 according to their residential air quality levels. Diagnoses considered were "pseudocroup" and obstructive bronchitis; pollutants were SO_2 and dustfall (g/m^2/day). Groups of high and low pollution were defined and tested by chi-square for significant differences in the numbers of

cases during the 4 years. For example, there were about twice as many croup cases when the average SO_2 exceeded 70 $\mu g/m^3$, compared to residential areas where the average SO_2 was less than 70 $\mu g/m^3$. For bronchitis, there were 2.5 times as many cases for areas with average dustfall exceeding 0.35 g/m^2/day [about 140 $\mu g/m^3$ as TSP (*115*)]. The authors ruled out confounding by residential density, viral epidemics, or meteorological influences. These findings are qualitatively consistent with those of Douglas and Waller (*113*).

Regional Comparisons of Hospital Utilization. Gornick (*117*) presents data on hospital use that allow some regional comparisons by diagnosis; these data are potentially of interest because air pollution in the United States also exhibits regional trends (*116*). The population studied was Medicare enrollees age 65 and over. The trend data show that from 1968 to 1977, for all diagnoses, admission rates increased and the average length of stay decreased nationwide. Patient-days peaked in 1969. Respiratory diagnoses increased slightly less than did all causes. The only detailed respiratory diagnosis analyzed was pneumonia, for which the average hospital stay was about 12 days and the median was 9 days; this difference indicates the influence of long-stay patients. By region the time trends were not greatly different, but regional differences persisted for most diagnoses and after adjustment for age, sex, and race. These differences were most pronounced for the long-stay patients and were seen in both surgical and medical cases. The Northeast tended to have the lowest discharge rates but the longest lengths of stays, but the North Central region had the highest values for "days of care per 1000 Medicare enrollees," which decreased slightly over the 10-year period. The West was lowest in both lengths of stay and days of care.

Using 1979 observations for 195 Professional Standards Review Organization areas, Gornick developed regression models for both lengths of hospital stay and discharge rates for Medicare enrollees age 65 and over (all diagnoses). The independent variables included average enrollee age, sex, race; physicians, short-stay hospital and nursing home beds per 1000 enrollees; percentage of area enrollees living in SMSAs (density); and the hospital occupancy rate. In addition, dummy variables were entered for the Northeast, North Central, and South Census Regions. The most important variables for lengths of stay were hospital occupancy rate, the Northeast and North Central dummy variables, and the number of short-stay beds; 83% of the variance was explained. For discharge rates, the most important variables were the number of physicians, short-stay beds, the South dummy variable, and the percentage of enrollees age 75 and over; 60% of the variance was explained. A model was not developed for patient care-days. Gornick explained the negative effect of the supply of physicians as the impact of alternative treatments other than hospitalization. This in turn could lengthen the average stay for those patients that are hospitalized. This analysis showed that both personal and economic variables played a role in hospital utilization and that some portion of the regional differences remained unexplained (which could be due to environmental variables, which were not included in this study).

Gornick also examined state level data in a previous analysis (*118*). In this work, the high admission and discharge rates in rural states were attributed to "distance to health care," which might favor inpatient rather than outpatient treatment. Personal factors (for example the low usage of tobacco and alcohol) were cited as being responsible for Utah's low rate of patient days (40% below the national average; see the discussion above of time-series studies in Utah). Since Utah also has low mortality rates, its low rate of hospital usage was also cited as an example that greater hospital use "is not directly related to higher health status" (*117*). Gornick's (unstated) hypothesis was apparently that greater hospital usage should lead to lower mortality, whereas the presence of excess risk factors in a population will lead to greater rates of hospitalization and mortality.

In 1990, the Health Care Financing Admistration published a geographic analysis of 1986 Medicare inpatient hospital services and the outcomes of treatment, by major diagnostic group and surgical procedure (*119*). The maps of hospitalization rates for all diagnoses, for heart disease, and for pneumonia and influenza are of interest to this review. Only the heart disease map showed a distinct regional pattern, similar to the mortality pattern (*120*), except that the high mortality zone extends somewhat to the north of the high hospitalization zone. The hospitalization patterns bear only a superficial resemblance to regional air pollution patterns (*121*), undoubtedly because there are many other factors involved.

Children's hospitalization rates in the United States and Canada were compared by Kozak and McCarthy (*114*). They found that overall and respiratory hospitalization rates were higher in Canada and that lengths of stay were longer there also. They attributed this trend in part to the higher availability of hospital beds. This is further evidence of the importance of supply factors in determining rates of hospital use.

Synthesis of Studies

Almost all of the studies reviewed found some statistically significant positive associations between air pollution and hospital use, although the correspondence between specific pollutants and specific diagnoses varied widely. It is possible that negative findings have been systematically excluded because of publication bias, even though the "gray" literature has been included in this review. However, there are some important differences among the studies that should be considered.

Selection of Dependent Variables

Diagnostic categories considered also varied among the studies. Only four investigators considered cardiac diagnoses, for example, and only two included eye complaints. The definitions of "respiratory" were inconsistent among

Table 2. Definitions of respiratory cases.

Investigators and site	Definition	% of total
Admissions (inpatients)		
Sterling et al. (*46*), Los Angeles, 1961	Includes upper respiratory and eye	3.7
Mazumdar and Sussman (*59*), Pittsburgh, 1972–77	All respiratory conditions	8.0
Pope (*64*), Utah County, UT, 1985–89	Asthma, bronchitis, pneumonia, pleurisy	4.3
Bates and Sizto (*8*), S. Ontario, 1976–82	No upper respiratory conditions	2.3
Plagionnakis and Parker (*112*), Ontario Counties, 1976–82	All respiratory diagnoses	7–13
Emergency room visits		
Ministry of Health (*14*), London, 1952	All respiratory	58
Namekata et al. (*57*), Chicago, 1977–78	Upper and lower respiratory separated	13
Durham (*49*), California, 1970–71	All respiratory diagnoses	24
Samet et al. (*58*), Steubenville, OH	All respiratory diagnoses	26

the various studies, as shown in Table 2. One study (*52*) did not specifically investigate respiratory diagnoses.

The fractions of total diagnoses classified as "respiratory" varied considerably among studies, especially between admissions and emergency room visits; part of this variation is due to definitional differences and part may be due to population or environmental differences. Admission to hospital requires an action by a physician, while a visit to an emergency room or clinic is based only on the subjective symptoms of the patient. The observation that respiratory diagnoses account for a higher fraction of emergency room visits than of admissions reflects the fact that respiratory symptoms may be more obvious to the patients than other types of complaints. One could also infer that this percentage increases drastically during severe air pollution episodes, which suggests use of percent of admissions (or emergency room visits) classified as respiratory as an analysis metric. For comparison with Table 2, the U.S. national average percentage of respiratory admissions was 9.35% (*122*); subtracting acute respiratory infections and chronic tonsil disease leaves 7.4%. Coffey (*123*) reported patient statistics by type of hospital and location inside SMSAs for 1977; public hospitals had proportionately fewer respiratory admissions inside SMSAs and more outside SMSAs, with an average of about 8% overall, not counting acute upper respiratory infections or tonsils/adenoids.

It is interesting to note from Table 2 that even in Los Angeles, which was a very polluted city in 1961, the sum of upper and lower respiratory admissions (percentages) was no greater than corresponding data from Toronto and the Utah Valley. Such comparisons suggest that cross-sectional comparisons of hospital usage will be difficult to interpret. As discussed above, factors relevant to the supply and delivery of medical care must be considered in relation to differences in long-term average rates.

Only two studies considered lengths of hospital stays (*47,109*). Given that admissions decisions may be based in part on factors other than the patients' needs, it would appear that environmental effects on lengths of stay should be given additional emphasis in future studies as an index of the severity of illness. Another possibility would be to use length of stay as a stratifying variable in conjunction with admissions data.

Comparisons of Time-Series Study Designs and Results

Table 3 presents summary information on the major time-series studies reviewed. Note that many studies did not explicitly control for seasonal cycles and only Fishelson and Graves (*55*) controlled for potential effects of holidays on hospital usage. The study by Lamm et al. (*66*), which linked a specific viral agent to seasonal cycles in pediatric hospitalization, provides justification for the need to separate climate-driven air pollution cycles from infection-driven illness cycles. However, in northern climates, use of temperature as an independent covariable will provide a certain amount of seasonal control.

Serial correlation was neglected by most authors; however, Fishelson and Graves (*55*) did not find this factor to be substantial, based on Durbin-Watson statistics. As indicated in Table 3, interpolating between pollution measurements in time may introduce serial correlation; conversely, leaving gaps in the data record due to missing observations may reduce serial correlation (*57*), but it also makes analyses of lag effects difficult.

The column "pollutant exposure" in Table 3 is my subjective judgment as to how well the monitoring data used in each study may represent the actual population exposure. Factors considered include the local versus regional nature of the pollutant, the numbers of monitoring stations used, and the way that interpolation was done. Indoor/outdoor air pollution relationships were not spatially considered and are potentially important, given that most people spend the majority of their time indoors (*127*). Note that poor characterization of exposure will usually lead to underestimation of effects. Another variable factor that affects the ability to detect a true effect is the number of observations, which varied from 20 for the smallest data set of Namekata and Carnow (*54*) to 1569 individual visits in the Portland study (*9*).

By pollutant, statistically significant associations were found for particulate measures (smoke, COH, PM_{10} or TSP), sulfur measures (SO_2 or SO_4^{2-}), and ozone, in most of the studies, even at very different concentration levels. There was little or no correspondence between the adequacy of the exposure estimation and the finding of statistical significance. Nitrogen dioxide was found to be

Table 3. Summary of major time-series studies of air pollution and hospital use.

Investigators	Area studied	Time period	Type of data	Confounding effects[a]				Serial correlation	Pollution level, $\mu g/m^3$	Adequacy of pollutant exposure	Significant associations[b]					Best lag, days
				Weather	Wind	Season	Other				Total	Resp	Cardiac	Cardiac + Resp	Other	
Martin (42)	London	Winters 1958–59 1959–60	Admissions	Y	Wind	Y			Smoke = 215	Poor	X(58-59)	X	X	X		NA
									SO_2 = 442	Poor	X(58-59)	X	X	X		NA
Sterling et al. (46)	Los Angeles	Mar–Oct 1961 (n = 223)	Admissions			?	Holidays	?	SO_2 = 34	Good				X	Eye + Resp	1,3
									NO_2 = 83	Good					Eye + Resp	1,3
									CO = 9ppm	?					Eye + Resp	3,4
									O_3 = 0.4ppm	Good				X	Eye + Resp	2,3
									Particulates	Good					Eye + Resp	3.5
Sterling et al. (47)	Los Angeles	Mar–Oct 1961 (n = 223)	Length of stay			?	Holidays	?	SO_2 = 34	Good			X	X	Eye + Resp	NA
									NO_2 = 83	Good			X	X	Eye + Resp	NA
									CO = 9ppm	?						NA
									O_3 = 0.4ppm	Good			X(−)	X(−)		NA
									Particulates	Good			X	X		NA
Durham (49)	Los Angeles San Francisco (7 universities)	Oct 1970–June 1971	Visits to student health centers			?		?	SO_2 = 13–50		X					
									NO_2 = 60–170		X					1
									CO = 5.7ppm							
									O_3 = 0.22–0.028ppm		X					2
									COH = 2–3 km							
Jaksch and Stoevener (9)	Portland, OR	1969–70 (n = 1569)	Admissions		X	?	Holidays	?[c]	TSP = 61	Poor						
		(individual)	Cost		X	?	Holidays	?[c]	TSP = 61	Poor		X				1
Seskin (52)	Washington, DC	1973–74 (n = 365)	Unscheduled visits			?	Holidays	?	O_3 = 0.14–0.18	OK					Eye	
									NO_2 = 85	OK						
									SO_2 = 37–150	Poor					Eye	
									CO = 7ppm	Poor						
Fishelson and Graves (55)	Chicago	1971–73 (n = 81)	ER visits			?		No	SO_2 = 60	Good		X*	X			1
									COH = 88	Good			X*			
Namekata and Carnow (57)	Chicago	1977–78 (n = 29–131)	ER visits			?	Holidays	No?	SO_2 = 25	Poor			X			
									NO_2 = 81	Poor						
									TSP = 76	Poor						
Kurt et al. (60,61)	Denver	Winter 1975–76	ER visits	Y	Y	Y		?	CO = 18ppm	Poor			X			1
Samet et al. (58)	Steubenville, OH	1974–77 (n = 249(	ER visits				Holidays	?	SO_2 = 90	OK		X				0
									TSP = 156	OK	X	X				0
									NO_2 = 40	OK						
Mazumdar and Sussman (59)	Pittsburgh	1972–77	Emergency, urgent adm.			Y		?	SO_2 = 65–120	Poor	X(?)	X(−)				NA
									COH = 60–130	Poor	X	X(?)	X			
Pope (65)	Utah Co., UT Salt Lake Co.	1985–89	Monthly admissions			?		?	PM_{10} = 46	Poor		X			Children	1 month
Bates and Sizto (8)	Southern Ontario	1974–78 (n = 240)	Admissions			?	Trend Holidays	?	SO_2 = 80[d]	Poor	X(W)	X(S)				1,2
									NO_2 = 90[d]	Poor	X(W)(−)					
									COH = 0.9[d]	Poor						
									O_3 = 0.06ppm[d]	Poor	X(W)(−)	X(S)				1,2
Bates and Sizto (72)	Southern Ontario	1976–82 (n = 416)	Admissions			?	Holidays	?	SO_2 = 80[d]	Poor		X(S)				
									NO_2 = 90[d]	Poor	X(S)	X(S)			Asthma	1,2
									COH = 0.9[d]	Poor	X(W,S)					
									O_3 = 0.06ppm[d]	Poor	X(S)	X(S)			Asthma	1,2
									SO_4^{2-} = 13.3	OK		X(S)			Asthma	1,2
Hammerstr et al. (11)	Southern Ontario	1979–85	Admissions			?	Holidays	No	SO_2 = 18	Poor		X				2
									NO_2 = 45	Poor						
									O_3 = 40	Poor		X				2
									COH = 0.4	Poor						
									SO_4^{2-} = 13	OK		X				3
									TSP = 75	Poor						
Bates et al. (75)	Vancouver, BC	1984–86	ER visits		Y	Y		?	SO_2 = 28 (max h)			X			Asthma	
									NO_2 = 78	OK		X			(61 +)[e]	1,2
									O_3 = 48		X					
									COH = 0.41						Asthma	
									SO_4^{2-} = 3.35			X			(61 +)	

Abbreviations: Resp, respiratory; ER, emergency room; TSP, total suspended particulates; NA, not applicable. [a]Y, confounding effect may have been present; X, significant association. [b](S) summer data (maximum values); (W) winter data (maximum values); X(−), significant negative association. [c]May have been introduced by interpolating for missing TSP data. [d]Average of peak summer values. [e]Significant only for the 61 + age group. *Significant for only one age group.

significant in Los Angeles, Southern Ontario, and several European cities, but not in Washington, Chicago, or Steubenville. Carbon monoxide was only studied in five locations (Denver, Los Angeles, Washington, Barcelona, and Helsinki) and was significantly associated with cardiovascular emergency room visits in Denver. Carbon monoxide tends to have poor exposure characterization because of the local nature of emissions. Carbon monoxide was associated with eye irritation in two studies, which seems counterintuitive [eye irritation is not mentioned in summaries of CO health effects (*124*)], although CO could be a surrogate for some other pollutant associated with primary emissions from vehicles. This may be the explanation for the association of CO with asthma in Helsinki and with COPD in Barcelona.

There is no obvious relationship between average pollutant concentration levels and significance of findings, but this may be due in part to the differences in study designs and execution.

By type of diagnosis, cardiac diagnoses were associated with SO_2, ozone, and fine particles (COH), but only a few studies considered cardiovascular disease. In contrast, considering the totality of studies reviewed, respiratory symptoms were associated with all pollutants. Respiratory admissions were associated with particulates in about half of the studies reviewed; SO_2 was also frequently associated with respiratory causes. Note that uncertainties in admission diagnoses may blur any specific disease-pollutant relationships that may have been present.

The lag column in Table 3 indicates that all daily studies which considered lags found them to vary between 1 and about 3 days, with the exception of the Steubenville study (*58*), which found the unlagged variables to fit better. However, only Fishelson and Graves (*55*) looked at cumulative lag variables, which is probably a better procedure since it better accommodates individual differences in responses. The finding of a 30-day lag in the monthly analysis of Pope (*64*) remains unexplained.

Quantitative comparison of the relative strengths of the associations found may be made from Table 4, which summarizes the various estimates of elasticity for the statistically significant pollutants (one at a time). It is difficult to make such estimates for the major episodes because the responses often did not proceed at a constant rate during the episode; but they appear to be much higher, in the range of 20–70%. Most of the elasticities in Table 4 are in the range of 5–20% (i.e., from 0.5 to 2% change in hospital use [for specified diagnoses] for a 10% change in air pollution). The high values obtained in Utah stand out from the other time-series studies; the analysis by Lamm et al. (*66*) showed that the fraction of increased hospitalization attributed to air pollution would decrease (to the range of the other studies) if the simultaneous presence of viral agents were considered. The low values found by Martin (*41,42*) may relate to the lack of consideration of lags. The elasticity values estimated from cross-sectional studies are reasonably consistent with the time-series findings [when one considers the high levels of air pollution present during the Douglas-Waller study (*112*)]; this implies that the cross-sectional studies may be measuring the annual sum of acute effects rather than chronic effects per se.

The relationship between mortality and hospitalization rates during air pollution episodes is also of interest. Certainly, it appears from some of the episode and time-series studies that hospitalization rates attributable to air pollution are of the same order of magnitude as excess mortality rates in terms of absolute numbers, which seems counterintuitive. For example, Mills (*125*) reports 22 deaths and 320 hospitalizations at the Poza Rica oil refinery episode and at Donora, Pennsylvania, he reported 20 deaths with 805 people treated by physicians and 338

Table 4. Comparison of elasticity estimates.

Author	Location	Significant pollutants	Elasticity[a]
Time-series studies			
Martin (*42*)	London	SO_2, smoke	6–7
Sterling et al. (*46*)	Los Angeles	SO_2, O_3	10
Durham (*49*)	California	SO_2, NO_2, O_3	7–10
Samet et al. (*58*)	Steubenville, OH	SO_2, TSP	4.5
Kurt et al. (*60,61*)	Denver	CO	32
Lutz (*62*)	Salt Lake City	TSP	70
Pope (*65*)	Utah Valley, UT	PM_{10}	67
Lamm (*66*)	Utah Valley, UT	PM_{10}	13
Bates and Sizto (*72*)	S. Ontario	SO_2, NO_2, O_3, SO_4^{2-}	8
Lipfert and Hammerstrom (*74*)	S. Ontario	SO_2, TSP, O_3, SO_4^{2-}	20
Knight (*78,79*)	Prince George, BC	reduced S, TSP	5–9
Sunyer et al. (*97*)	Barcelona	SO_2, CO, smoke	9–19
Ponka (*92*)	Helsinki	NO, NO_2, O_3, CO	12
Schwartz et al. (*100*)	5 German cities	SO_2, NO_2, TSP	2–17
Cross-sectional studies			
Carpenter et al. (*109*)	Pittsburgh	SO_2, TSP	17
Douglas and Waller (*113*)	England and Wales	SO_2, smoke	40
Plagionnakis and Parker (*112*)	Ontario	SO_2, SO_4^{2-}	13–36

TSP, total suspended particulates.

[a]Elasticity values are given in percentage units and are for individual pollutants, as opposed to joint regressions on combinations. See text for additional qualifications. Dependent variables include both admissions and emergency room visits.

others "trying unsuccessfully to get medical aid." It appears that there also were more hospitalizations than deaths associated with the toxic release at Bhopal, India, as was the case with a recent subway fire in Brooklyn (*126*). Accounts of the 1952 episode in London suggest that many more people were affected than either died or sought to be hospitalized. Thus it is not clear how to interpret the apparent statistical finding that excess mortality may be a more sensitive indicator than "excess" hospitalizations. Part of the explanation may be associated with differences in health status; at least some portion of the excess deaths may be premature by only a few days or weeks, whereas the emergency hospitalizations may represent a different portion of the population (especially children).

Discussion

This review of approximately 100 studies involving air pollution and demands for hospital services has shown that these demands can be useful end points for quantifying effects on community health. Hospital data tend to be less subjective than symptom data and have the advantage that, unlike mortality, a trip to the hospital is not an inevitable outcome and thus the degree of prematurity is not an issue. Useful data have been obtained from studying both admissions and emergency room visits; their relative utility may depend on access to data and to the nature of the population being studied. In some central city areas, emergency rooms are being used for primary care (*91*).

As in all studies of the adverse effects of air pollution, there are three main questions of interest: *a*) Is there a causal relationship linking air pollution to the adverse effect? *b*) With what certainty can one distinguish which pollutant(s) are responsible? *c*) What are the dose–response relationships? The first question involves issues of study design, and the last question may involve issues of lagged responses and thresholds of no effect.

Comparisons among these many studies is hampered somewhat by their diversity; they vary in design, diagnoses studied, lag periods considered, and the ways in which potentially confounding variables were controlled. Study designs have evolved considerably over the 40 years of published findings on this topic. The early studies tended to emphasize the need to limit the populations studied to those living near air pollution monitors. More recent studies (*8,93*) employed the concept of regional pooling, in which both hospitalization and air monitoring data are pooled over a large geographic area. An important, mostly unfulfilled, need is to determine the long-term effects of changes in air quality, in addition to daily variations.

Additional insights might be gained by comparing precise replications of a given study protocol at a specific location over a time period with changing air pollution levels or for different cities having widely varying average air quality levels. The only study reviewed featuring such replication was that of Schwartz (*100*), who studied five German cities; differences in responses were observed among the five cities and these patterns were not seasonally dependent. Hospitalization studies may be more difficult in the United States because of the lack of suitable national databases.

The first of the above questions is undoubtedly the most difficult, and in a sense it is linked to the others. If specific physiological hypotheses cannot be generated and confirmed by clinical or laboratory research, the finding of nonspecific pollutant effects or poorly defined dose–response relationships raises the question that some other type of biological responses might be involved, such as those resulting from the meteorological conditions leading to air stagnations, for example. Some studies found significant negative associations (mainly for the diagnoses ostensibly unrelated to air pollution): is one justified in ignoring these while viewing the positive relationships as causal?

One must also note that, because factors associated with the supply of medical care appear to play an important role in hospital utilization, identification of the specific roles of environmental factors should be geared to elucidating information about the underlying health of the population, perhaps from data on symptom prevalence. Data on lengths of hospital stays may also be useful in this regard. The possibility that limitations on the supply of beds could also influence the timing of admissions should be considered.

Conclusions

Significant associations were found across a variety of study designs. The diversity in these study designs leads to the overall conclusion that an association has been shown between hospital use and air pollution, the lack of identification of a single "responsible" pollutant notwithstanding.

Table 4 shows that SO_2 and various measures of particulates (including SO_4^{2-}) were identified most frequently. Many studies found that the effects of SO_2 and particulates could not be separated; however, particulates were found to have an independent effect [Mt. St. Helens (*35*), forest fires (*40*), Utah Valley (*62,64–66*)], SO_2 was also found to have an independent effect [Vancouver (*75*), Koln (*100*), Honshu (*102*), Ontario (*112*)], and One study [Helsinki (*92*)] found that neither SO_2 nor smoke was significant. Ozone was also identified in several studies, but its effects tend to be seasonal. The probability that a given pollutant may in fact have an independent causal effect should also be considered in the light of indoor/outdoor air-quality relationships, since people spend so much of their time indoors.

Most of the studies were limited to linear models and thus pollutant thresholds could not be readily identified. However, comparisons across studies failed to reveal any obvious thresholds. These results thus could be used in cost–benefit studies as linear dose–response functions, if a probabilistic approach were adopted towards weighting the likely effects of the various alternative responsible pollutants.

These review findings also suggest that children's respiratory admissions should be examined separately,

especially in winter. For example, Bates and Sizto (*72*) found no significant air pollutant associations with children's asthma in Ontario and positive effects due to temperature in winter, while Pope (*64*) and Lamm et al. (*66*) showed negative temperature effects, corresponding to the seasonal trend or perhaps due to space-heating emissions from wood stoves. Kraemer and McCarthy (*35*) examined asthma admissions for ages 0–19 in Spokane and showed no consistent seasonal pattern or association with particulates (TSP), aside from the Mount St. Helens perturbation; there was no substantial lag effect apparent from this volcanic eruption episode (the total seasonal respiratory admissions variation was much less than in Utah, however).

Additional methodological recommendations from this review include the following. *a*) In time-series studies, a common averaging time should be used for all pollutants. *b*) There is no evidence that regional pooling of admissions and air quality data leads to spurious results. *c*) Cumulative lags up to at least 3 days should be considered and serial correlation should be accounted for. *d*) Respiratory diagnoses should be given priority, but cardiac cases should be included as well. *e*) It is essential to correct for seasonal, day-of-week, and holiday effects. No single best method of doing this has been identified; perhaps more than one technique should be used, in order to demonstrate robustness. *f*) Attempts should be made to account for indoor/outdoor air quality relationships. *g*) Studies should be made of the long-term effects of air pollution abatement on rates of hospital use.

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